SYNTHESIS AND DECOMPOSITION OF ARYL AZIDES

Thesis presented in Candidature for the degree of

Doctor of Philosophy

of the

University of Salford

by

Winston Anthony Strachan

Department of Pure and Applied Chemistry

University of Salford

August 1974

ACKNOWLEDGEMENTS

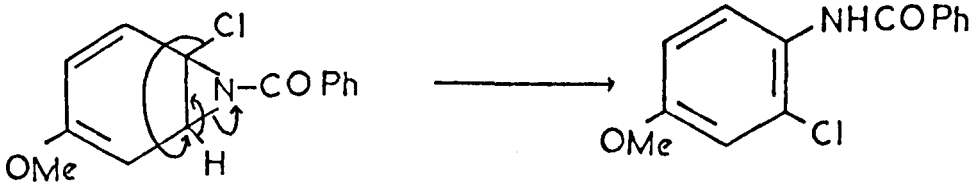
The author would like to express his sincere thanks to Dr. R.K. Smalley and Professor H. Suschitzky for their advice, encouragement and patience during the course of this work.

The author is also indebted to the Science Research Council for a Research Studentship.

CONTENTS

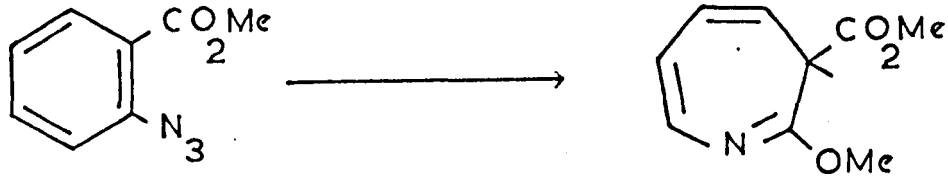
SUMMARY

Aryl azides have been thermolysed and photolysed in benzoyl chloride to give azo compounds, anilides and ortho chlorinated anilides (e.g. 2). The formation of these latter products has been investigated mechanistically and it has been shown that chlorination of the aromatic system arises neither by radical nor electrophilic chlorine attack but by chloride ion migration via an aziridine intermediate (1) as shown below.



(1) (2)

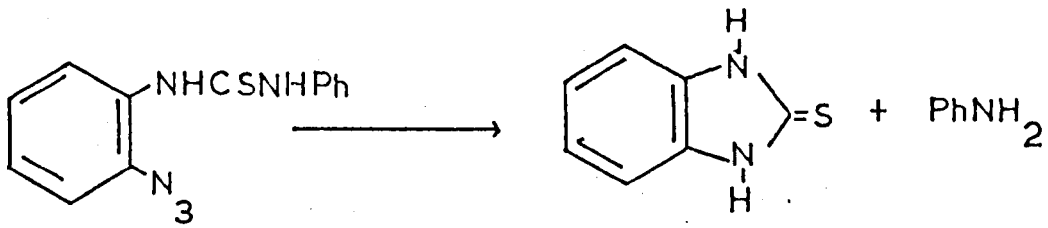
o-Azido-carbonyl compounds (e.g. 3) have been thermolysed in inert solvents and have given mainly polymeric materials. However, photolysis in alcohol has given 2-Alkoxy-3H-azepines (e.g. 4) in high yields.



(3) (4)

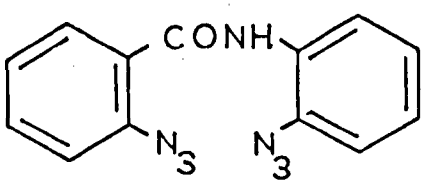
The 3H-azepines have been shown to be derived from singlet nitrenes via azirine intermediates which are attacked by the alcohols followed by ring expansion.

o-Azidoanilino derivatives have also been thermolysed in inert solvents to give mainly amines and tars. However, in some examples interesting products have been formed i.e. the formation of benzimidazole-2-thione (6) from N'-(2-azidophenyl)-N-phenyl-thiourea (5). This has been shown to arise via N'-(2-aminophenyl)-N-phenyl thiourea.



(5) (6)

Photolysis of the o-azidoanilino derivatives in methanol has given only amines. Some diazides (e.g. 7) were also synthesised .



(7)

but these on photolysis in methanol were found to be either unaffected or gave polymeric materials.

The novel reaction of methyl o-azidobenzoate with hydrazine hydrate in ethanol to give indazoline-3-one has been investigated, and a mechanism has been proposed to explain indazolinone formation.

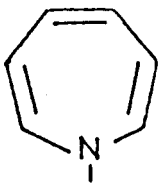
INTRODUCTION

C H A P T E R 1

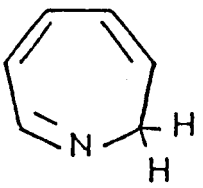
SYNTHESIS OF AZEPINES

(a) Structure and Nomenclature

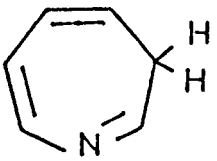
Azepines are seven-membered unsaturated heterocycles of substantial pharmaceutical interest. The framework of these ring systems contains six carbon atoms, one nitrogen and seven hydrogen atoms. As a result four isomeric parent systems exist (1-4).



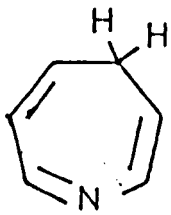
(1)



(2)



(3)



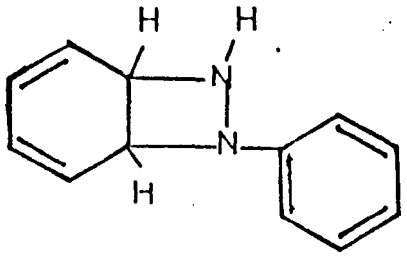
(4)

The numbering of these heterocycles is done by referring to the particular structure in question and indicating the position of the odd hydrogen atom with a locant followed by an italicized H. Thus structures (1-4) become the 1H-, 2H-, 3H- and 4H- azepines respectively. All four isomers are non-aromatic. In fact the 1H- azepine which is characterised by a cyclic array of 8π-electrons and which differs from the monocyclic system with $(4n + 2)\pi$-electrons, has been shown to be non-aromatic by Schmid.[1] Calculations based on Hückel molecular orbital concepts show that this isomer has a strong polyene character accompanied by localization of theπ- electrons on nitrogen and double bonds, but very little tendency for delocalization, one of the main features of aromaticity.

No examples of the 2H-azepine system have been reported, whereas the other isomers in particular the 3H-, and the 1H-azepines are well known and their synthesis is discussed in the following section.

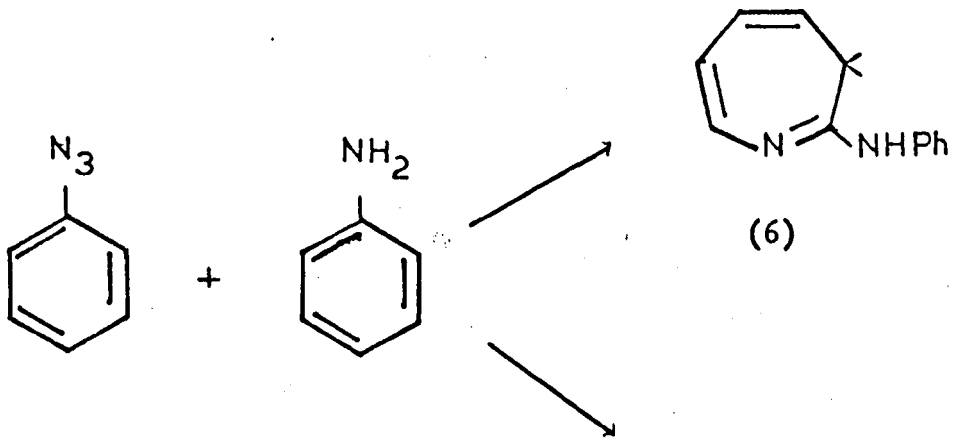
(b) Azepines by Decomposition of Aryl Azides

Wolff [2] in 1910 obtained a compound from the pyrolysis of phenyl azide in aniline, which he called dibenzamil, and which was thought to have a diazetidine structure (5).

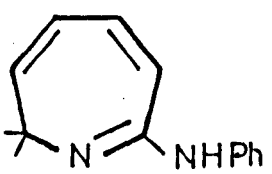


(5)

It was not until 46 years later that Huisgen and co-workers [3,4,5,6] showed that Wolff's dibenzamil was in fact a 7-membered ring containing an amidine system and which was formulated either as 2-anilino-3H-azepine (6) or 2-anilino-7H-azepine (7).



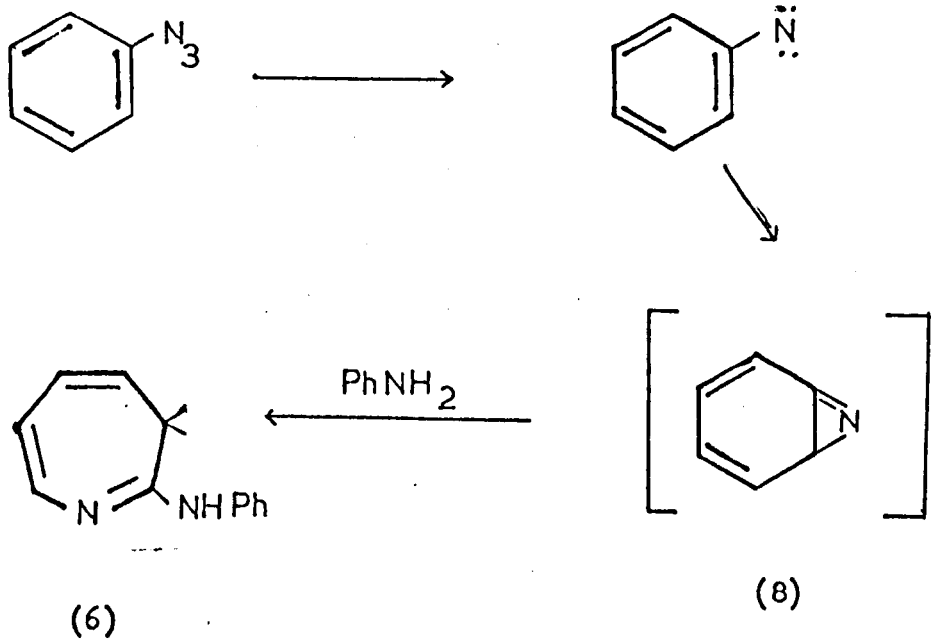
(6)



(7)

Appl and Huisgen [6] proposed a mechanism for the formation of the cyclic amidine which involved initial formation of an azacyclopropene intermediate, namely 7-azabicyclo [4:1:0] hepta-2, 4, 6-triene (8) which later reacted with aniline to form the seven-membered ring as indicated in Scheme 1.

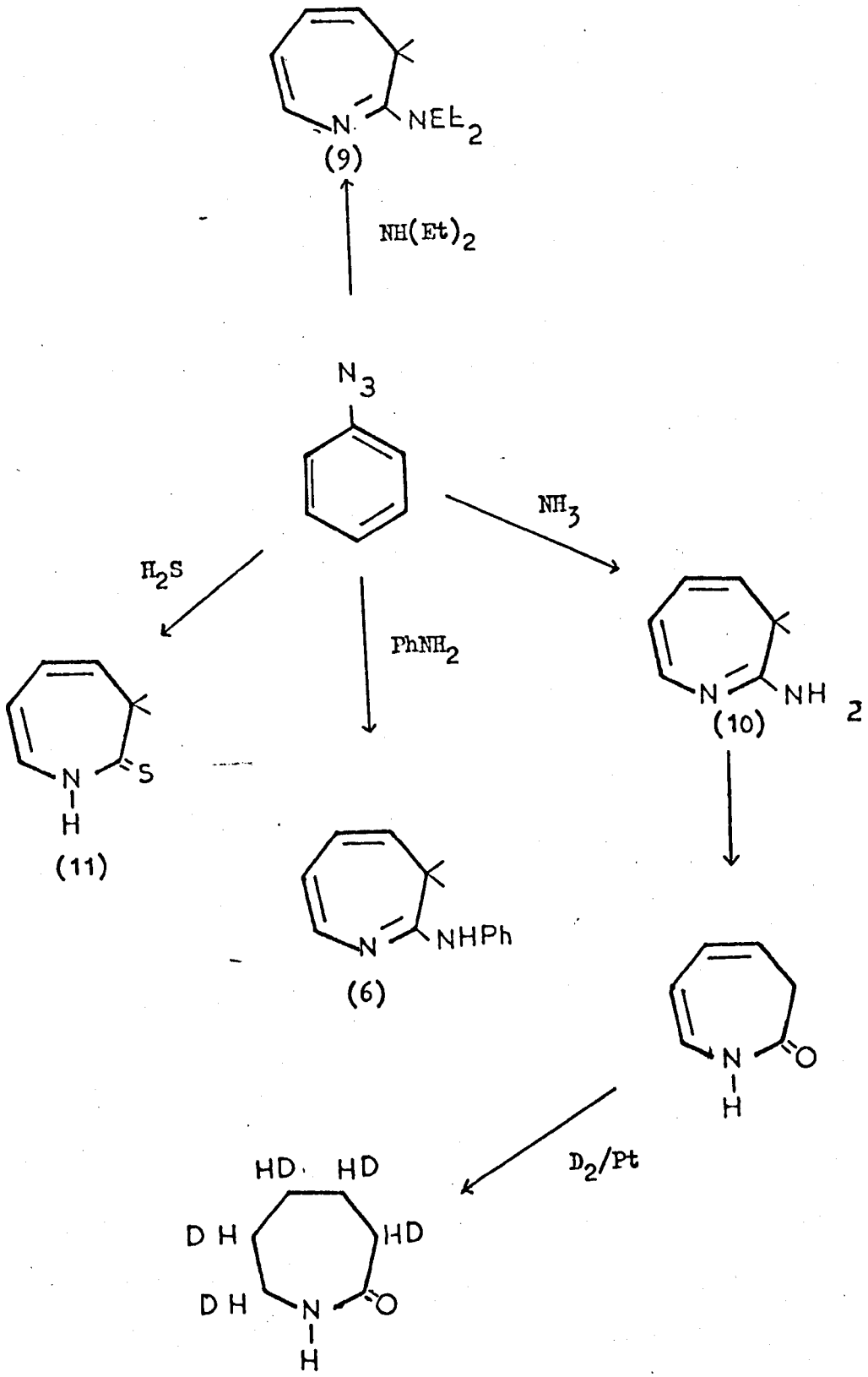
SCHEME 1



(6) (8)

Subsequently Doering and Odum [7] examined the photoreaction of phenyl azide in the presence of bases and other nucleophiles. They found that on irradiating phenyl azide in aniline, diethylamine, or liquid ammonia, 2-anilino-3H-azepine (6), 2-diethylamino-3H-azepine (9) and 2-amino-3H-azepine (10) respectively, were isolated. Treatment of phenyl azide with hydrogen sulphide gave a small yield of 1,2-dihydro-2-thienoketo-3H-azepine (11). These reactions are summarised in Scheme 2.

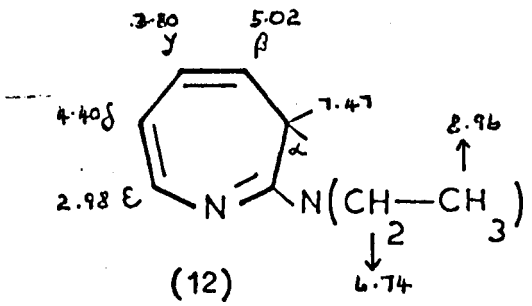
SCHEME 2


NEt2
(9)
NH(Et)2
N3
NH3
H2S
PhNH2
NH2
(10)
S
(11)
NHPh
(6)
O
D2/Pt
HD HD
D H
HD
D H
O

The structure of these cyclic amidines was established chemically by hydrogenation and subsequent hydrolysis to the ε-amino caproic acid and the corresponding base. The ultraviolet spectra were similar to that of acetamidine, and the absence of -NH- absorption in the infra red spectra together with strong absorption at 1600 cm^{-1} were in accord with the proposed structures.

In fact the most important evidence in proving the structure of these 3H-azepines came from ^1H nuclear magnetic resonance spectra.

The distinctions between the 3H-azepine (9) and its possible alternative structure i.e. the 7H-azepine was elucidated by arguments based on chemical shifts.



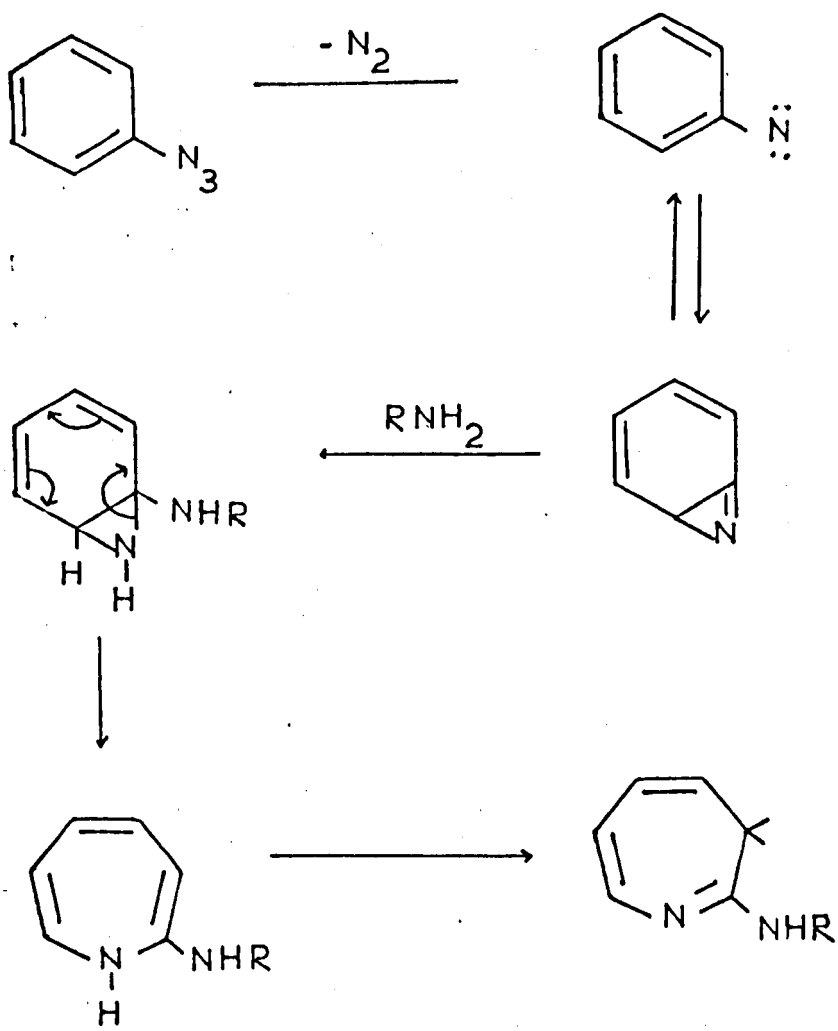
(12)

If it was the 7H-isomer then $C_\varepsilon H$ would be α to the amidine carbon atom while $C_\delta H$ would be β. In α,β-unsaturated nitriles, acids, aldehydes and ketones, the β-hydrogen is always shifted to a lower field than the α-hydrogen. Also the $C_\delta H$ would be at a lower field than $C_\varepsilon H$, which is contrary to the evidence (see diagram).

Similarly for double bonds attached to atoms with unshared electrons, the α-hydrogens appear at low field [8] and if the structure was the 3H-isomer then $C_\varepsilon H$ would be shifted further downfield, as in fact is observed. Hence on the basis of the magnetic resonance evidence the 3H-isomer is the most consistent structure of the two.

One of the main problems in the formation of azepines by photolysis of phenyl azide in bases [6,7] is to determine whether the 3H-azepine is formed via the 1H-azepine as had been suggested by Maier. [9]

SCHEME 3



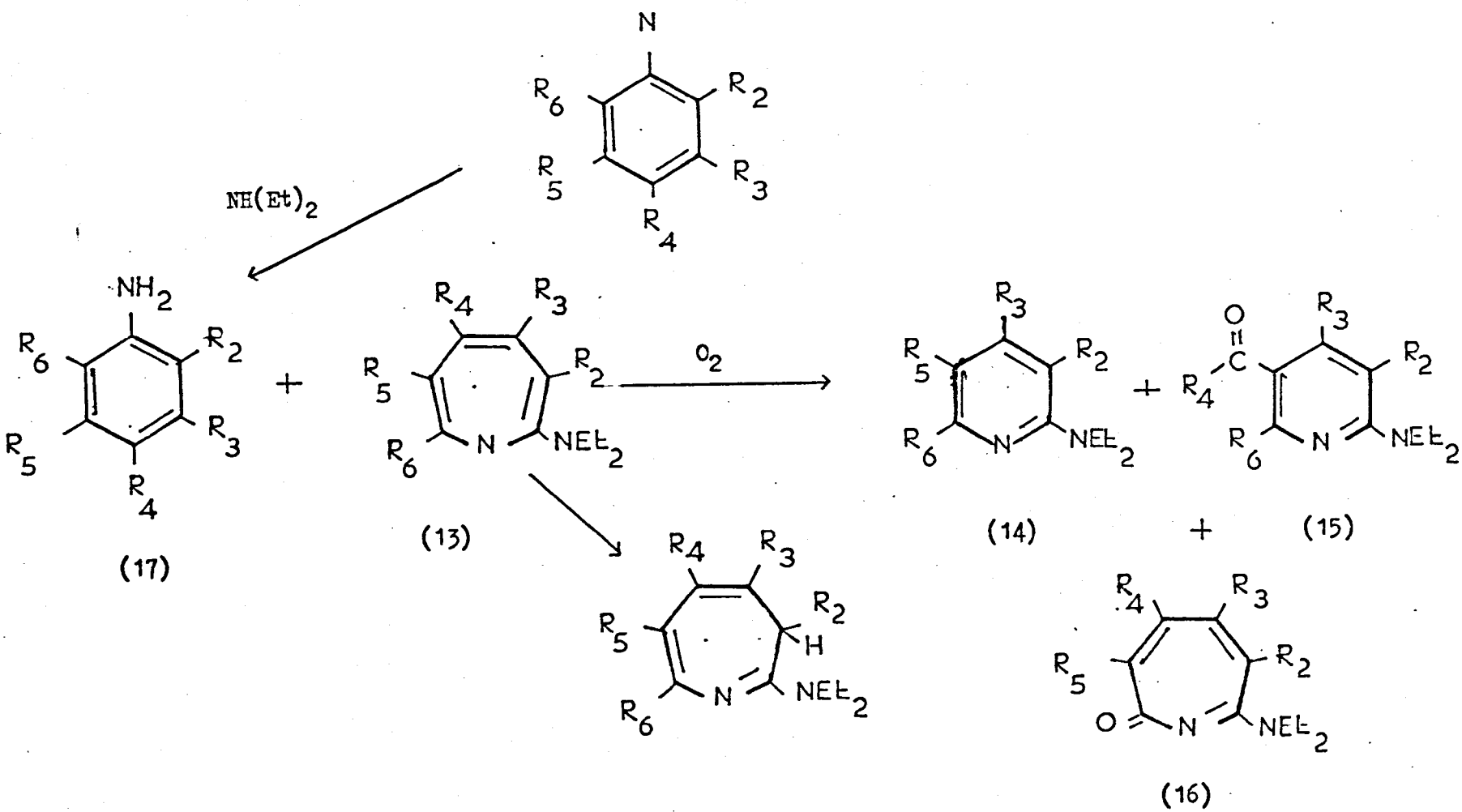
The first workers to show that these 1H-intermediates existed were Sundberg, Suter and Brenner.[10] They photolysed a series of ortho substituted aryl azides in diethylamine and showed that these led mainly to oxygen sensitive metastable intermediates formulated as 1H-azepines (13) rather than to 2-diethylamino-3H-azepines which are commonly obtained from such photolyses. They also showed that the products identified as 3-alkyl-2-diethylaminopyridines (14), 5-acyl-3-alkyl-2-diethylaminopyridines (15) and 6-alkyl-7-diethylamino-2H-azepin-2-one (16) as outlined in Scheme 4 arose by oxidation of these oxygen-sensitive 1H-azepines intermediates, and not by breakdown of the 2-diethylamino-3H-azepines.

Table 1a

Photolysis of Substituted Aryl Azides in Diethylamine

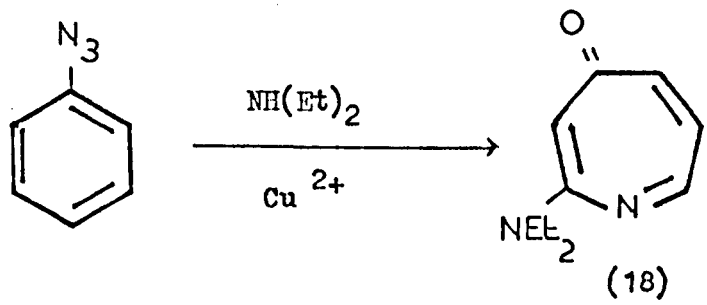
	R_2	R_3	R_4	R_5	R_6
a	H	H	H	H	H
b	CH_3	H	H	H	H
c	CH_3	CH_3	H	H	H
d	CH_3	H	CH_3	H	H
e	CH_3	H	H	CH_3	H
f	CH_3	H	H	H	CH_3
g	CH_3	H	CH_3	H	CH_3
h	H	H	CH_3	H	H
i	C_2H_5	H	H	H	H
j	i-C_3H_7	H	H	H	H
k	i-C_3H_7	H	H	H	CH_3
l	C_6H_5	H	H	H	H

SCHEME 4



In fact in some cases (azides e and j) when oxidation of the intermediates were carried out in the presence of cupric ion 6-alkyl-7-diethylamino-4H-azepin-4-one (18) were produced.

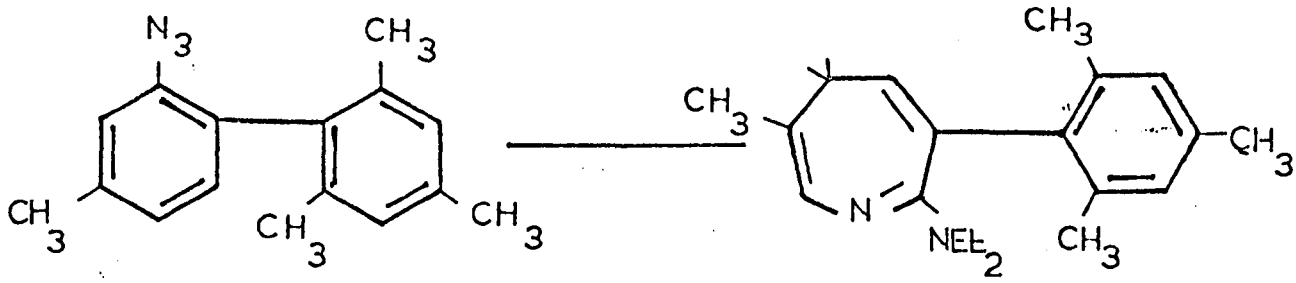
SCHEME 5



(18)

^{1}H nuclear magnetic resonance spectral data indicates that these oxygen-sensitive intermediates are 3-alkyl-2-diethylamino-1H-azepines (13). When azides lacking ortho substituents e.g. phenyl azide and p-tolyl azide were employed no evidence for the analogous 1H-azepine formation was obtained. The explanation given was that these intermediates were too short lived to be detected. Also an azide bearing an ortho-mesityl substituent namely: 2-azido-2',4,4',6'-tetramethylbiphenyl (19) gave 7-diethylamino-3-methyl-6-(2',4',6'-trimethylphenyl)-4H-azepine (20) as the primary product and here again there was no evidence for the oxidisable intermediate.

SCHEME 6



(19) (20)

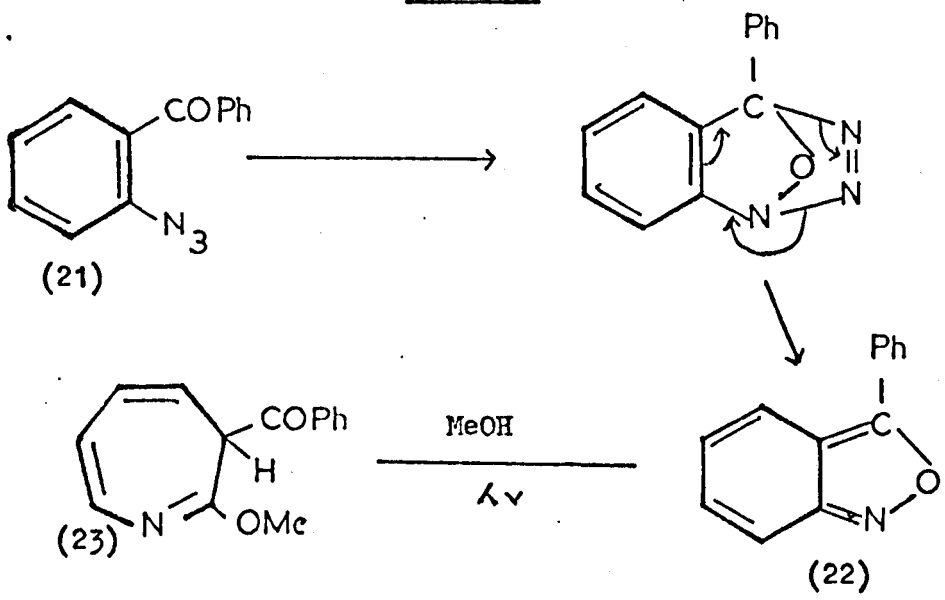
Finally these workers concluded that the 3H-azepines were formed via the 1H-azepines and it was the latter and not the former which ring contracted to form the aminopyridines or rearranged to give the 2H-azepin-2-ones.

The synthesis of 3H-azepines from the photolysis and thermolysis of aryl azides [6,7,11] has been thoroughly investigated, but little success has been achieved in trapping the postulated azirine (8) by nucleophiles other than amines. Recently, however, a few reports concerned with the trapping of the azirine by methanol have appeared.

Smith [12] and his co-workers showed that thermolysis of 2-azidobenzophenone (21) in chlorobenzene gave 3-phenylanthranil (22). Later, Hall, Behr and Reid [13] showed that this reaction does not involve a "pure" nitrene but is assisted and probably occurs by way of a 1,3-dipolar cycloaddition.

Ogata, Kăño and Matsumoto [14] have shown that 3-phenylanthranil, obtained from the azide (21), on photolysis in methanol yields 3-benzoyl-2-methoxy-3H-azepine (22) (58%). These reactions are summarised in Scheme 7.

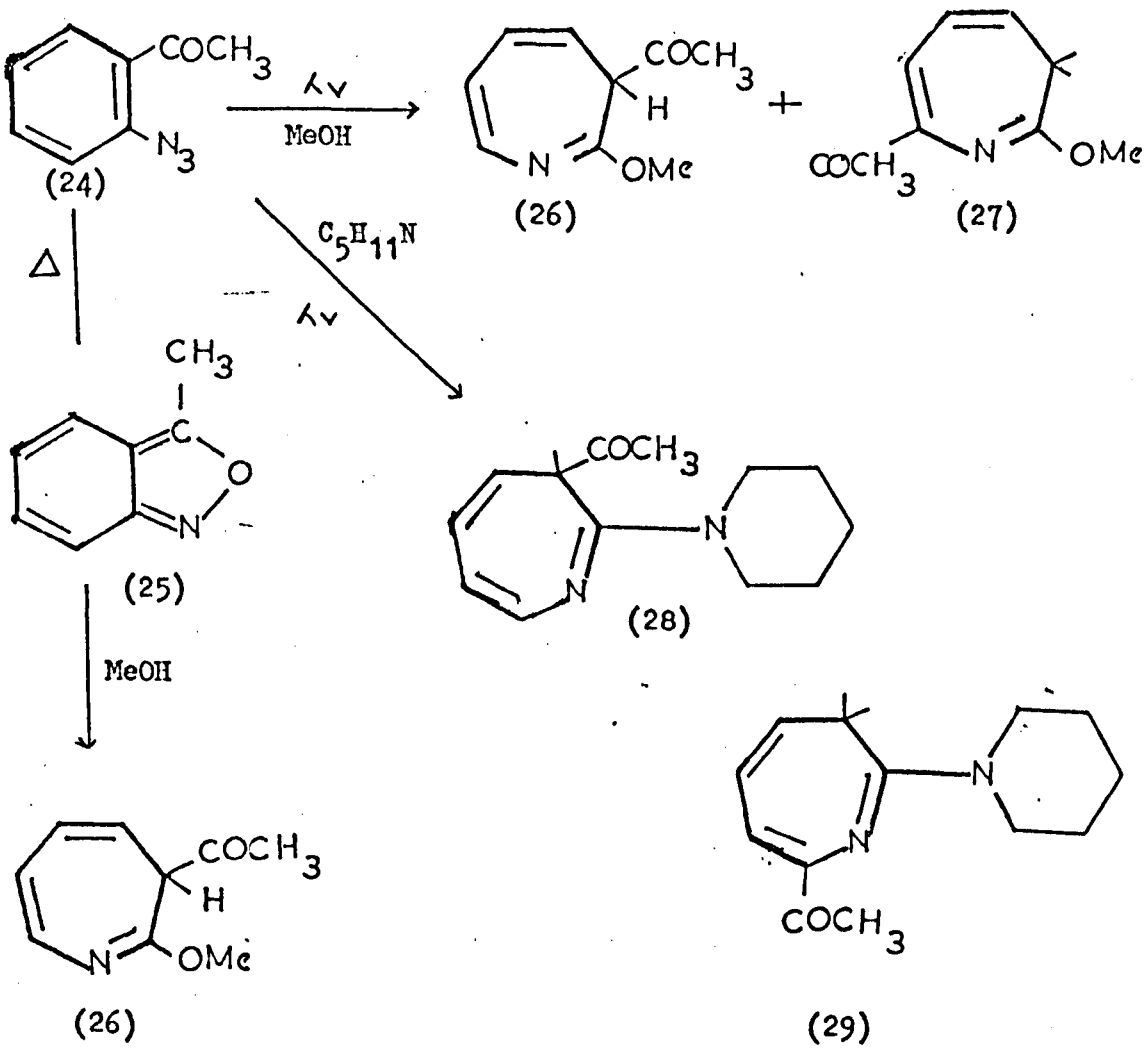
SCHEME 7



Berwick [15] in order to explain the relationship between the anthranil and the azide took 2-azidoacetophenone (24) and 3-methylanthranil (25) and investigated their photolytic decomposition in methanol. 3-Methylanthranil on photolysis gave 3-acetyl-2-methoxy-3H-azepine (26) in 56% yield, whereas the azide (24) gave the 3H-azepine (26) together with a small amount of another isomeric azepine which was assumed to be 7-acetyl-2-methoxy-3H-azepine (27). The mixture proved to be inseparable and the structures were allocated on the basis of ^{1}H n.m.r. spectra. However when the azide (24) was photolysed in piperidine, 3-acetyl-2-piperidino-3H-azepine (28) was formed together with an equal amount

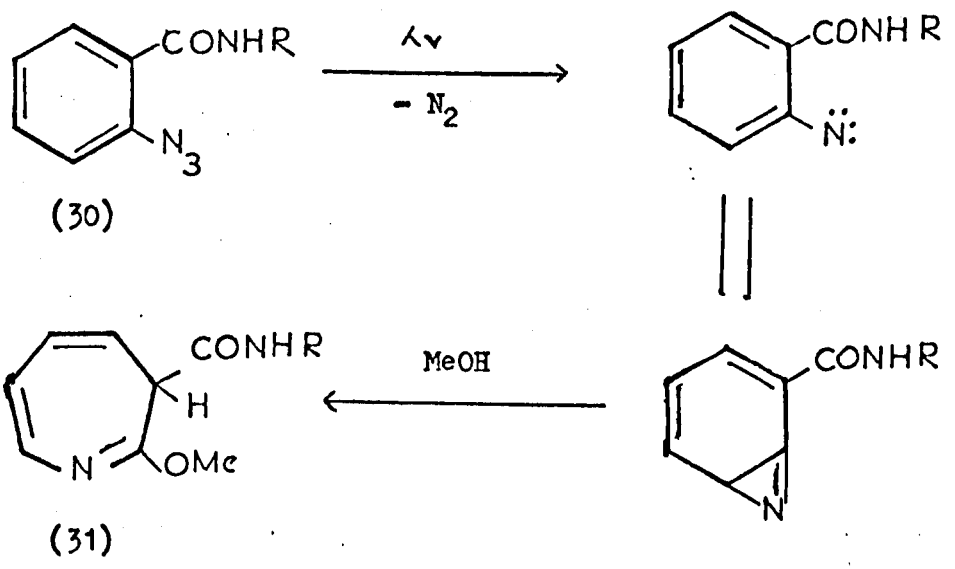
of a new azepine, 7-acetyl-2-piperidino-3H-azepine (29). This author also investigated the e.s.r. signals given by the azide (24) and the anthranil (25) in a solvent matrix at -196° in the presence of a triplet sensitiser and found that in the case of the azide, a triplet nitrene was detected whereas in the case of the anthranil it was absent. He then concluded by indicating that the nitrene from the azide (24) was reversible whereas the anthranil was not and although the reactions seem to proceed via azide-anthranil-azepine, the pathways differed from a standpoint of multiplicity, reversibility and selectivity.

SCHEME 8



It has been known for some time that N-Benzoyl-L-phenylalanine ethyl ester is a substrate for α-chymotrypsin [17] and a recent paper by Mair and Stevens [16] in a search for an irreversible inhibitor of this enzyme, have photolysed a series of o-azidobenzamides in methanol. For example, the prepared N(o-azidobenzoyl)-L-phenylalanine ethyl ester and the related o-azidobenzamides are shown in Scheme 9.

SCHEME 9



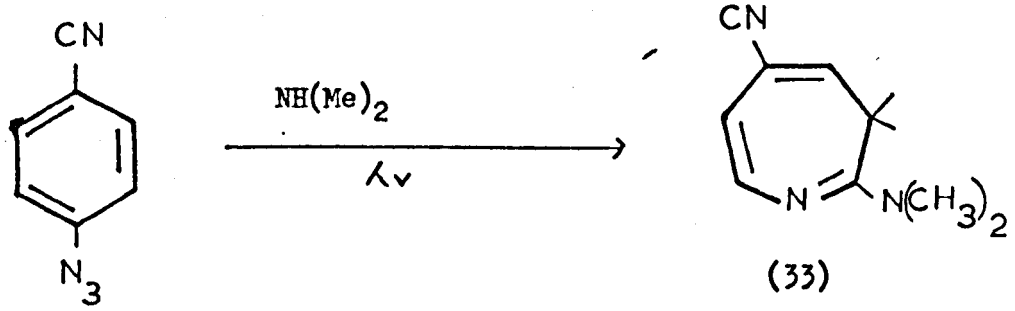
(30)

(31)

		Yield of Azepine
(a)	R = H	21
(b)	R = Me	41
(c)	R = Et	40
(d)	R = $Ph(CH_2)_2$	52
(e)	R = $CH(CO_2Et)CH_2$ R (L.configuration)	36

In each case varying amounts of 2-methoxy-3H-azepines (31) were formed and once again the reaction was postulated to proceed via a nitrene - azirine pathway as indicated in the reaction scheme. From these results they were able to show that a suitably substituted azide complexed at the active site of the α-chymotripsin could undergo photo-induced covalent interaction with a suitably positioned nucleophilic amino acid at the catalytic site of the enzyme.

Finally, Odum and Wolf [18] have recently reported that increasing the wavelength of light during photolysis of p-cyano-phenylazide (32) results in an increased yield of 5-cyano-2-dimethylamino-3H-azepine (33). This result was rationalised in terms of excess excitation energy producing a "hot" nitrene which gave an increased yield of the 3H-azepine (33).



(32) (33)

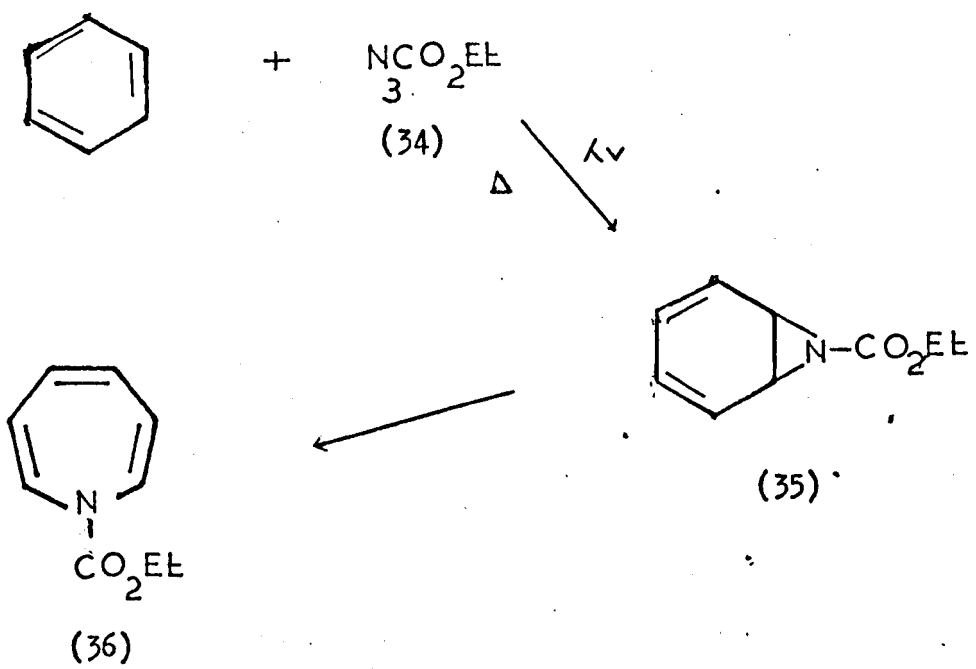
(c) Azepines from other azides RN_3 (where R = sulphonyl ethoxycarboxyl-, etc)

So far only aromatic azides have been discussed and the main feature in their reactions to give azepines is the availability of suitable nucleophiles which add on to the azirine intermediate followed by ring expansion. When aromatic azides are photolysed or thermolysed in aromatic solvents no azepines are formed and the usual products are azo-compounds and amines. These products have been rationalised by several workers [7,19] to have come from a triplet nitrene in contrast to the formation of the azepines which are derived from singlet nitrenes, as will be discussed later.

In the presence of non-protic aromatic solvents the triplet nitrenes can form azo-compounds or they can hydrogen abstract to form amines. An increase in the hydrogen availability of the solvent leads to an increase in the formation of the amines. When other azides e.g. ethoxycarbonyl-, sulphonyl- are thermolysed or photolysed in aromatic systems 1H-azepines are produced.

The first synthesis of a 1H-azepine was accomplished by photolysis and pyrolysis [20,21,22] of ethyl azidoformate (34) in benzene solution. This ring enlargement was rationalised to have occurred via an aziridinobenzene intermediate (35) as indicated in reaction Scheme 10 and gave 1-ethoxycarbonyl-1H-azepine (36) in good yield.

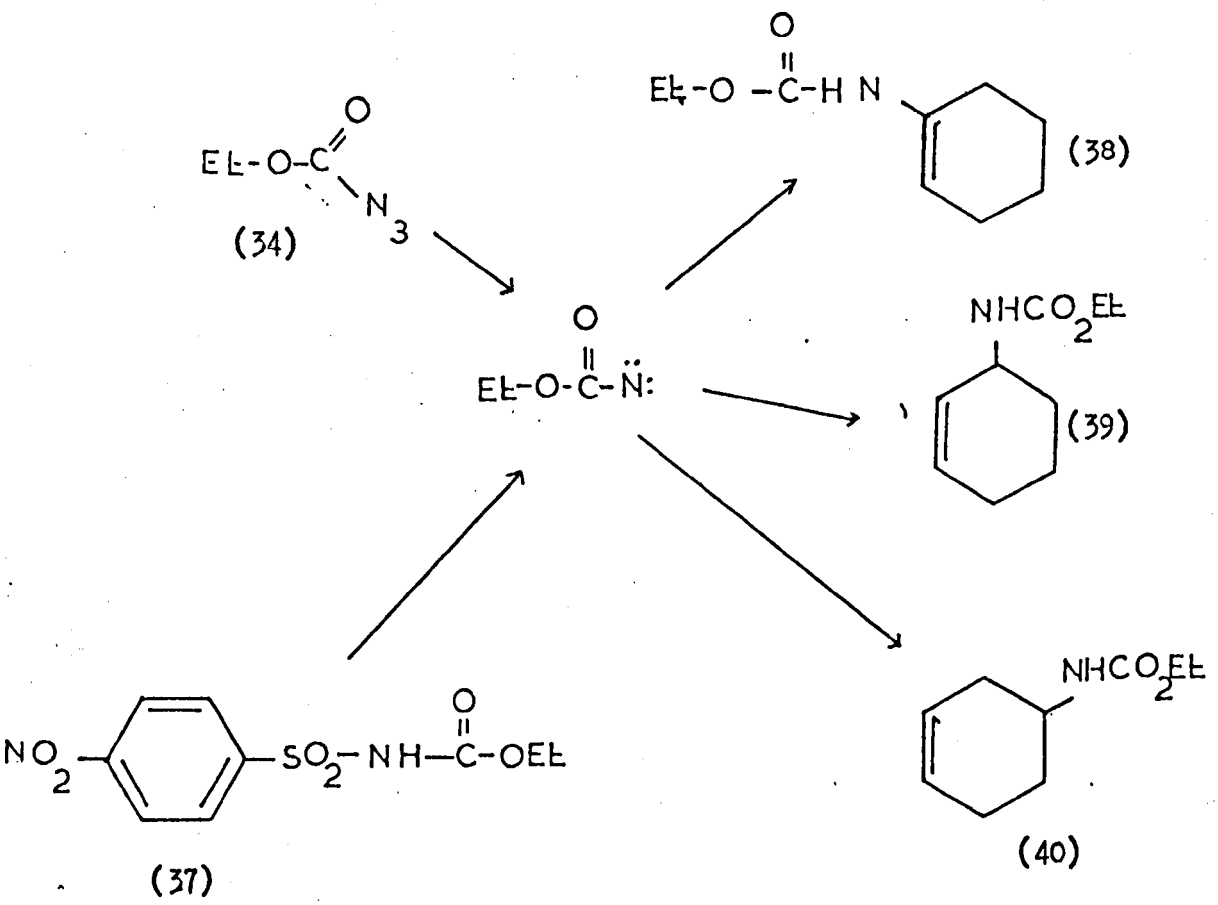
SCHEME 10



Decomposition of such electron deficient azides in the presence of benzene has become an important route to the synthesis of this ring system.

Lwowski and Maricich [22] investigated whether it was the carbethoxynitrene or the precursor ethyl azidoformate that led to the 1H-azepine (36). The intermediate was obtained from the anion of N-p-nitrobenzenesulphonoxyurethan by a base catalysed elimination and when the urethan (37) and the azide (34) were photolysed in various solvents, in particular cyclohexene, the ratio of the olefin addition products to the C-H insertion products indicates that the same species is involved in both addition and insertion reaction, hence proving that the carbethoxy nitrene leads to the formation of the 1H-azepine. These reactions are summarised in the following Scheme (11).

SCHEME 11



Lwowski and Johnson [23] have provided the evidence to show that it is the singlet nitrene which leads to the formation of the 1H-azepine (36). This was accomplished by comparing products obtained after decomposing the urethan (37) in molar concentrations of benzene/cyclohexane mixture and benzene/cyclohexene mixture (see Tables 1 and 2). It has been shown by these workers [24] that a singlet nitrene inserts into C-H bonds, while both singlet and triplet nitrenes will add to carbon-carbon double bonds. [25] From the results obtained the authors concluded that the products listed in

Table 1 were derived from the same nitrene species, while the products in Table 2 were produced from different species. Further the singlet carbethoxy nitrene converts benzene to N-ethoxy-carbonyl-1H-azepine, while both singlet and triplet nitrenes add to the double bond in cyclohexene.

Table 1

Reactions of carbethoxy-nitrene with benzene and cyclohexane

Conc. (mole %)		Yields (%)		Rates
Benzene	Cyclohexane	Azepine	Urethan	I/(I + II)
32	32	20	20	0.50
22.5	22.5	20	19	0.52
5	5	8.2	6.7	0.55
2.5	2.5	7.7	3.8	0.67
1	1	3.4	2.2	0.61
0.5	0.5	4	2	0.67

Table 2

Reactions of carbethoxy-nitrene with benzene and cyclohexene

Conc. (mole %)		Yields (%)		Rates
Benzene	Cyclohexene	Azepine	Aziridine	I/(I + II)
32	32	28.8	5.67	0.34
5	5	29.3	57.3	0.34
0.5	0.5	4.5	33.8	0.045
0.1	0.1	TRACE	16.4	v.s.

N-labelling studies with cyanogen azide have likewise shown [26] that N-cyano-1H-azepine is formed from a symmetrical intermediate. [27]

Other N-substituted-1H-azepines prepared by similar methods are shown in Table 3.

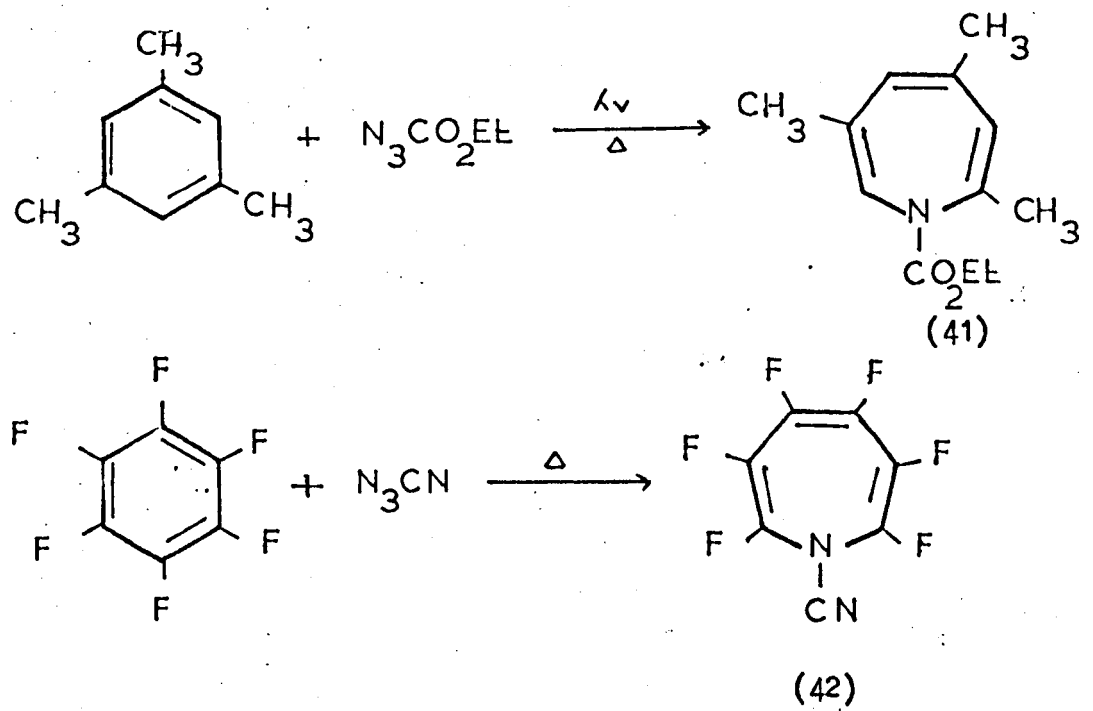
Table 3

N-Substituted-1H-azepine prepared by azide decomposition

Substituent on Nitrogen	Prep	Yield %	BPt/MPt(°C)	Ref
$-CO_2Et$	hν	70	130(20mm)	20
$-CO_2Et$	Δ	41	56(0.1mm)	28
$-CO_2CH_3$	Δ	33	63(0.05mm)	29
$-CO_2-C(CH_3)_3$	Δ	15	85(0.5mm)	30
$-CON_3$	Δ	-	-	31
-CN	Δ	70	48(0.2mm)	27

The drawback in the formation of these 1H-azepine derivatives is the lack of selectivity of the nitrene in its reaction with mono-substituted benzene. Usually isomeric 1H-azepines are produced which are extremely difficult to separate.[27,32] As a result of this, the synthesis has not allowed for the specific introduction of one or more substituents at different positions in 1H-azepine systems. Exceptional examples[26,27] are shown in Scheme 12 where in fact symmetry considerations simplify matters.

SCHEME 12



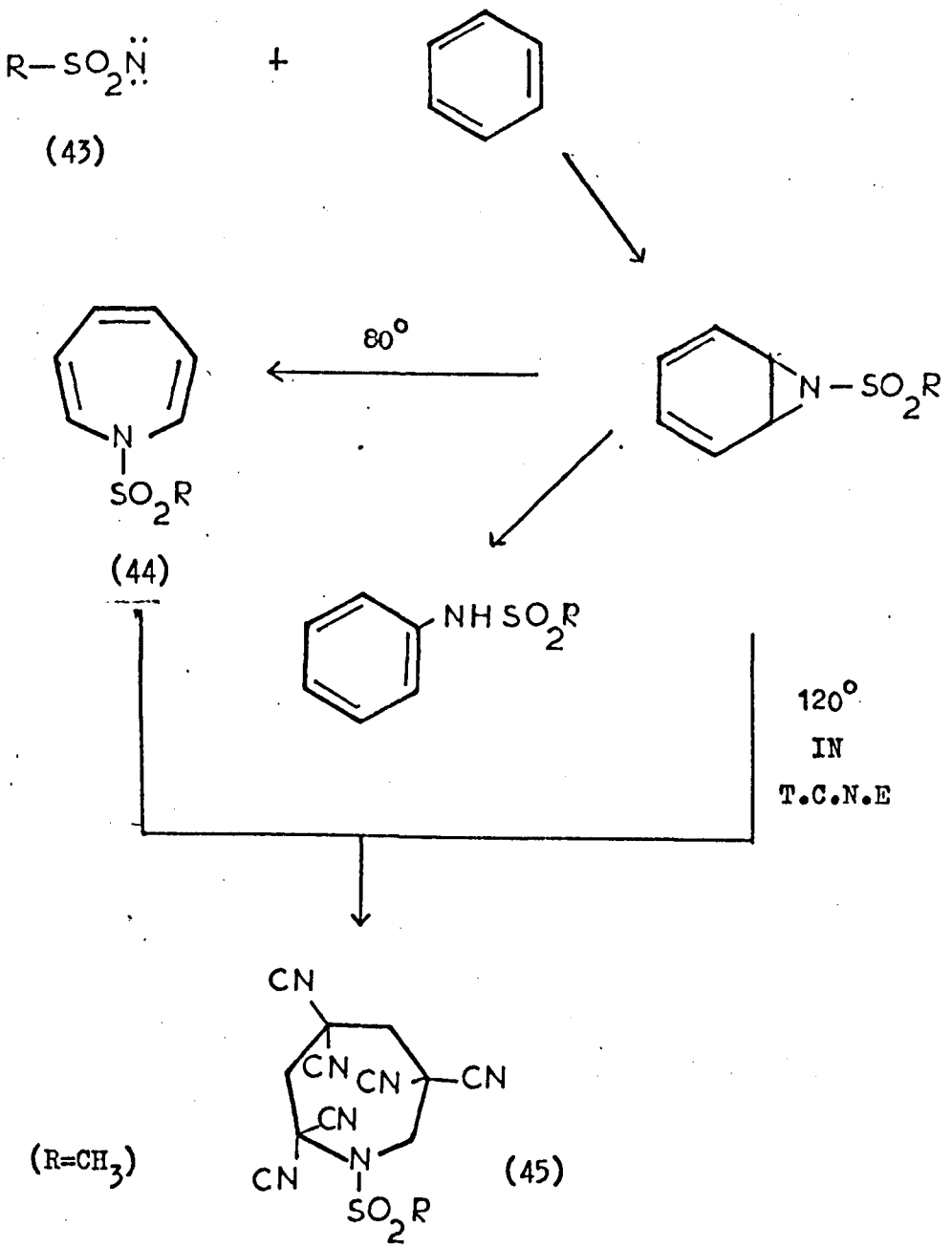
A puzzling feature of the reaction of sulphonyl azides with aromatic compounds is the formation of anilides as these have been rationalized as originating via an aziridine intermediate as shown in Scheme 12.

When carbethoxy-nitrenes react with aromatic solvents, 1H-azepines are produced whereas sulphonyl nitrenes yield anilides. This result is of interest since both arise from aziridine intermediates.

Abramovitch and Uma [33] showed that in fact a 1H-azepine (44) (see Scheme 13) is actually formed during the thermolysis of methanesulphonylazide (43) in benzene, and when the decomposition was carried out at 120° C in the presence of tetracyanoethylene (T.C.N.E.) the T.C.N.E. adduct (45) was formed at the expense of the anilide (46).

In fact, on carrying out the reaction at 80° C for 100 hrs, the presence of the 1H-azepine (44) was confirmed by thin layer chromatography. This azepine could be made to react with T.C.N.E. to give the adduct (45).

SCHEME 13



An explanation for the formation of this 1H-azepine (44) was rationalized in terms of an energy barrier. At 80^{o} the optimum energy needed to maintain the stability of this azepine was reached. Above this temperature more energy was being supplied to the system and this resulted in ring contraction of the azepine to form the anilide.

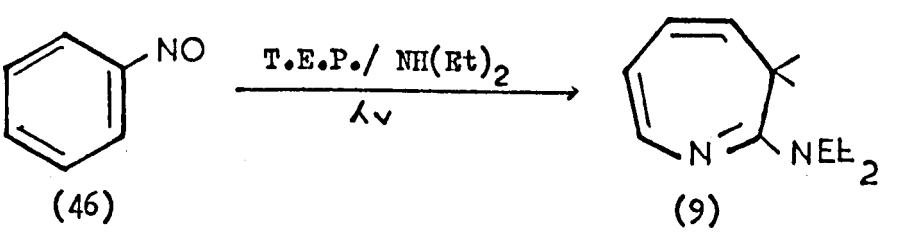
Thus the sulphonyl nitrene is in fact similar to the carbethoxy nitrene and the only difference is that the 1H-azepine formed from the latter is more thermally stable than the 1H-azepine formed from the former.

(d) Azepines from Nitro and Nitroso- Compounds

Since the discovery of the reaction in 1962 by Cadogan and Cammeron-Wood, [34] the reduction of aromatic nitro compounds by triethyl phosphite and related reagents has been exploited as a route to various nitrogen heterocycles including carbazoles, [35] indoles, [35,36] benztriazoles, [36] anthranils, [37] phenothiazines, [37,38] quinolines [39] and related compounds. Most of these heterocycles can be obtained by thermolysis of the corresponding azides [12,40,41,42] and with the exception of anthranils, a nitrene mechanism has been invoked to explain their formation from both the azides and nitro precursors. It was not surprising, therefore, that azepines could be obtained from nitro and nitroso compounds.

The first workers to report the formation of an azepine by this reductive technique were Odum and Brenner. [43] They reduced photolytically nitrosobenzene (46) with triphenyl and tributyl-phosphines in the presence of diethylamine and obtained 2-diethylamino-3H-azepine (9) as illustrated in Scheme 14.

SCHEME 14



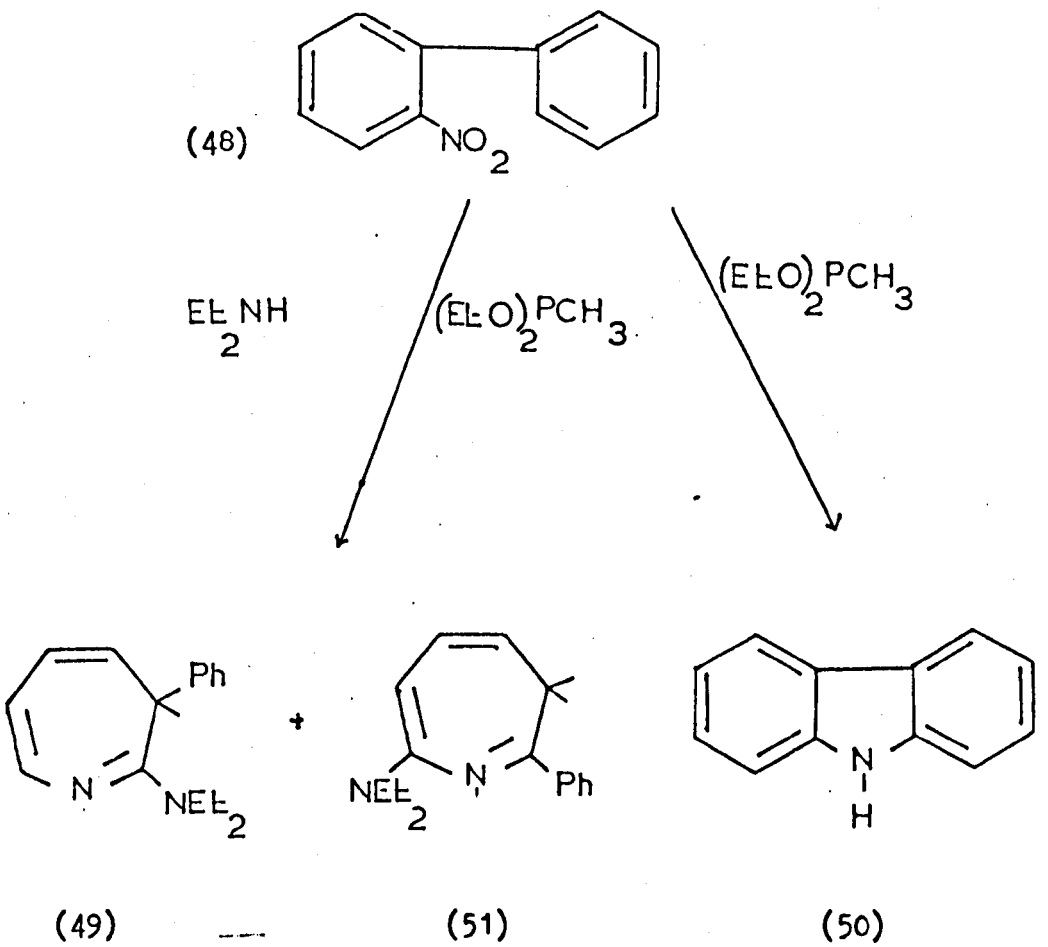
(46) (9)

Further work in this field was consolidated by Cadogan and Todd [44] and Sundberg and his co-workers. [45]

Cadogan and Todd [44] elegantly used Huisgen's mechanism to show that a nitrene participated in the triphenyl phosphite deoxygenation of nitrobenzene. Application of this test to the nitro-compound was difficult owing to the drastic conditions that had to be employed. However, the difficulty disappeared with the demonstration of the high reactivity of diethylmethyl phosphonite $(EtO)_2PMe$ as a reducing agent.

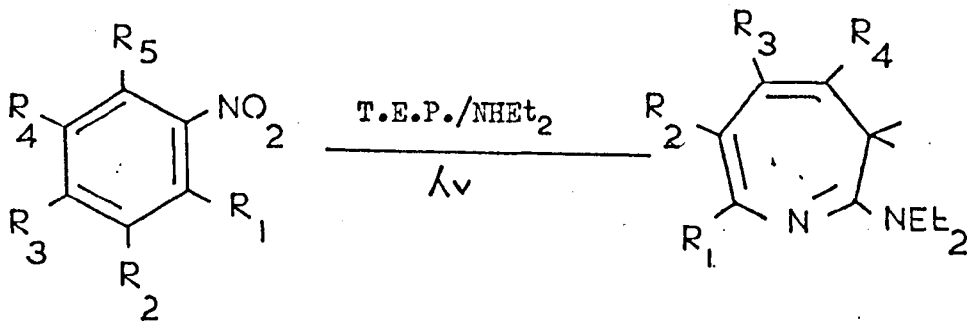
Nitrobenzene was then thermolysed in the presence of this reagent, in excess diethylamine and 2-diethylamino-3H-azepine (47) was obtained in 83% yield. The corresponding reduction of 2-nitrobiphenyl (48) in diethylamine gave 2-diethylamino-3-phenyl-3H-azepine (49) (13%) and carbazole (50) (67%). In the absence of diethylamine the yield of carbazole rose to 86%. A trace of the isomeric azepine, 7-diethylamino-2-phenyl-3H-azepine (51), was also detected. These reactions are summarised in Scheme 15.

SCHEME 15



Since isolation of the 3H-azepine (49) suggests participation of a nitrene mechanism, together with carbazole which again is rationalized to involve a nitrene mechanism, Cadogan and Todd suggested that the reduction of these nitro-compounds may involve a nitrene mechanism as shown by the reaction scheme. Sundberg and his co-workers [45] reduced certain nitrobenzenes with triethyl phosphite in the presence of diethylamine and obtained variable amounts of 2-diethylamino-3H-azepines. The results are summarised in Table 4.

Table 4



	R_1	R_2	R_3	R_4	R_5
a	H	H	H	H	H
b	CH_3	H	H	H	H
c	CH_3	H	CH_3	H	CH_3

Like Cadogan and Todd, they rationalized that the reaction proceeded via a nitrene mechanism. Subsequently, Cadogan and Mackie [46] thermolysed ortho-, meta-, and para nitrotoluenes, ortho-, and para ethylnitrobenzene and ortho and para nitroanisoles with triethyl and trimethyl phosphite. In the majority of cases azepines were formed as dialkyl alkyl-3H-azepin-7-ylphosphonates but the yields were very low ($\leq$ 18%). The results are shown in Table 5.

Table 5

Phosphorus containing azepines (%) of the reaction $ArNO_2 + (RO)_3P$

Ar	R	Azepine %
C_6H_5	Et	TRACE
o-Me C_6H_4	Me	18
o-Me C_6H_4	Et	85
m-Me C_6H_4	Me	TRACE
m-Me C_6H_4	Et	-
p-Me C_6H_4	Me	9
p-Me C_6H_4	Et	-
o-Et C_6H_4	Et	7
p-Et C_6H_4	Et	-
o-MeO C_6H_4	Me	-
m-MeO C_6H_4	Me	15
p-MeO C_6H_4	Et	-

Other advances in this field include the work done by Atherton and Lambert [47] who reduced substituted nitrobenzenes thermolytically with various trivalent phosphorus reagents in the presence of primary and secondary amines as outlined in Schemes 16 and 17.

SCHEME 16

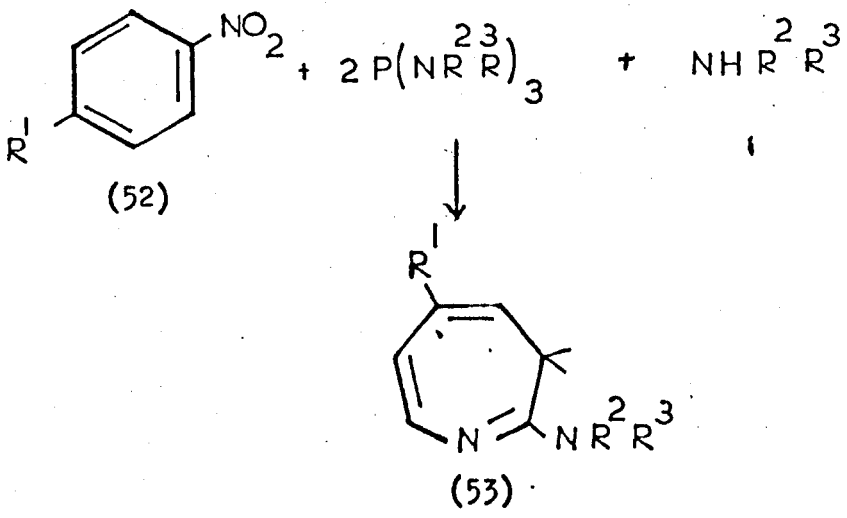
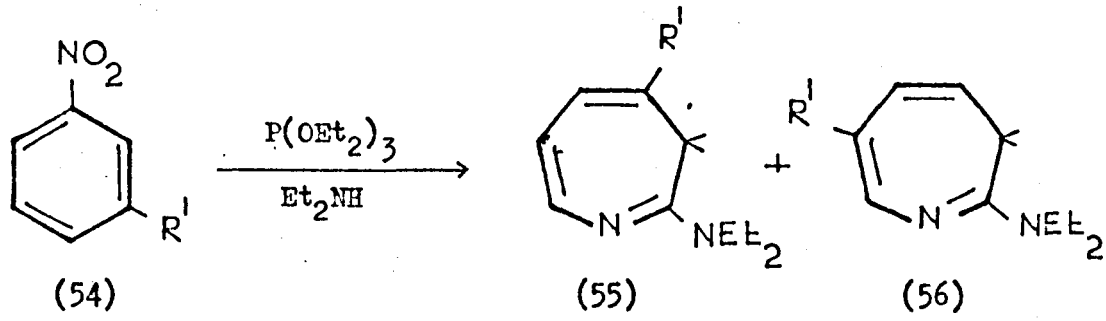


Table 6

Reduction of Nitrobenzenes by alkylphosphorus triamides in the presence of amines to give azepines

R^1	NR^2R^3	Yield %
H	piperidino	60
Me	$N(Me)_2$	42
Ph	$N(Et)_2$	56
4 Pyridyl	$N(Et)_2$	47

SCHEME 17



(54) (55) (56)

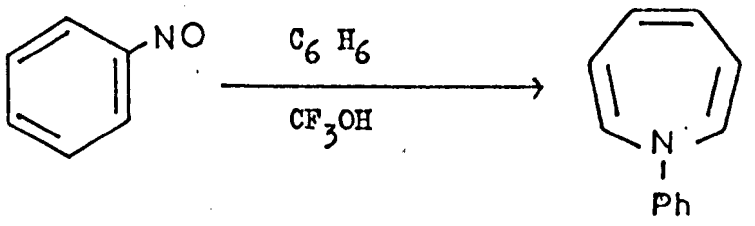
Table 7

Reduction of m-nitrobenzene to 4- and 6-substituted 3H-azepines

R^1	4-isomer %	6-isomer %
Cl	5	28
Ph	18	31
4-Pyridyl	19	30
Me	28	19
OMe	30	-
Et_2NCO	17	3
Ac	4	3

On the basis of the results given in Table 7 these authors were able to conclude that electron withdrawing groups in the meta-position of the nitrobenzenes favour the production of the 6-substituted 3H-azepines (56) whereas electron donating groups favour the formation of the 4-substituted isomer (56). Also when the substituents were in the para-position of the nitrobenzenes only 5-substituted-3H-azepines (53) were formed.

More recently Sundberg and Smith [48] have reported the first example of the formal addition of a phenyl nitrene to benzene to give 1-phenyl-1H-azepine (57). This was achieved by deoxygenation of nitrosobenzene with triethyl phosphite in a mixture of benzene and trifluoroethanol. The orange solid obtained, which had an imperical formula $C_{12}H_{11}N$ was identified as the 1H-azepine (57) on the basis of ^1H n.m.r. and ultra-violet data. In the presence of an acid the azepine rearranged to give diphenylamine.



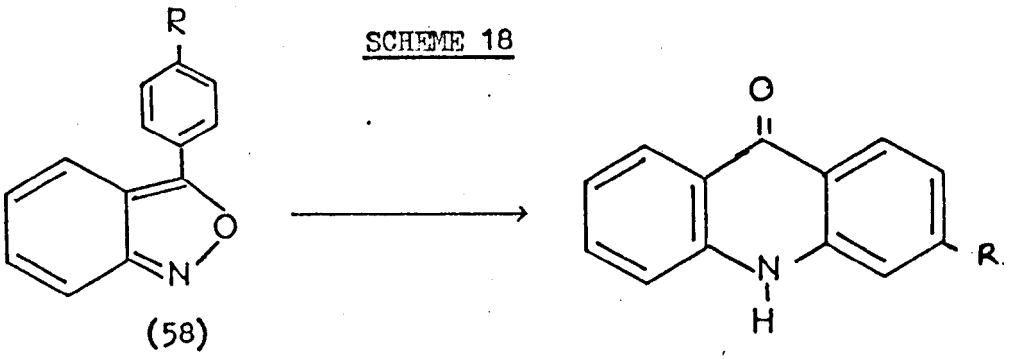
(57)

(e) Miscellaneous

(i) From Anthranils

It has been known for some time that methoxylated phenylanthranils [49] rearrange under pyrolytic conditions to give acridones in which the nitrogen is para instead of meta to the methoxy function.

SCHEME 18



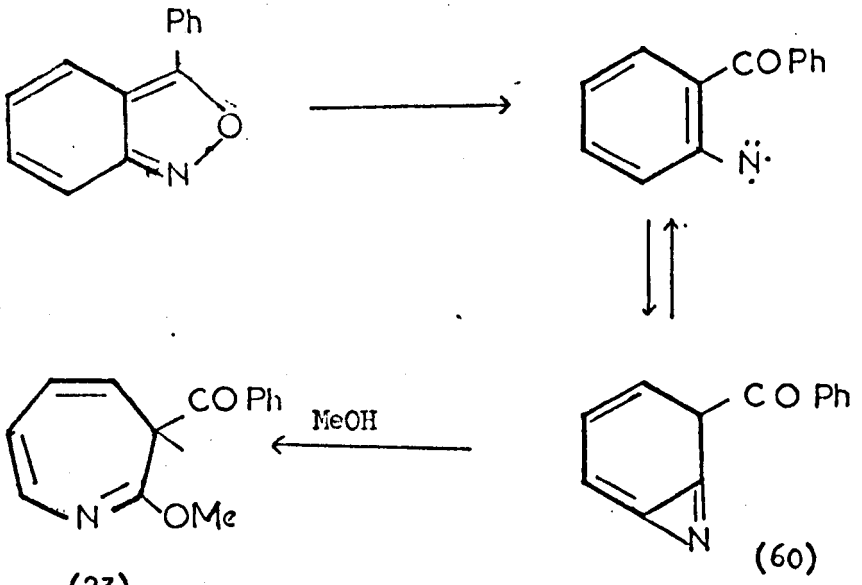
(58) (59)

R = alkyl or halogen

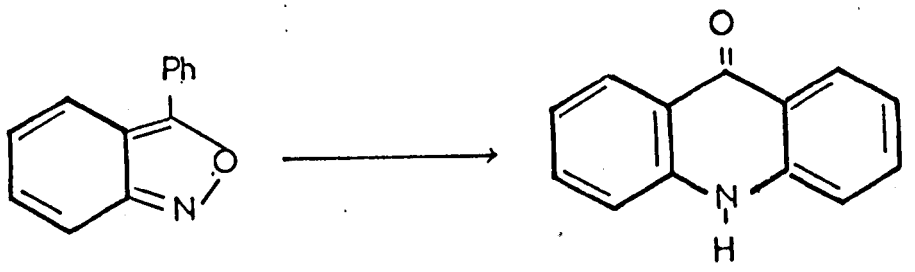
In the presence of nitrous acid, the methoxylated anthranils yield substituted azoxybenzoic acids instead of the anticipated acridones and a nitrene was proposed as the intermediate in this rearranged reaction.

In 1968 Ogata and his co-workers [14] photolysed 3-phenylanthranil (21) in methanol and obtained 3-benzoyl-2-methoxy-3H-azepine (22) in (58%) yield. They argued that this photoarrangement initially involved N-O bond cleavage to give an aryl nitrene which then undergoes ring closure to give the stable azirine (60) which on addition of methanol followed by ring expansion gave the azepine (23) as indicated in Scheme 19.

SCHEME 19



The idea was backed up by the fact that if the anthranil was substituted in the 7-position, no azepine was formed. Instead intramolecular cyclisation to give 9H-acridone (61) was observed.

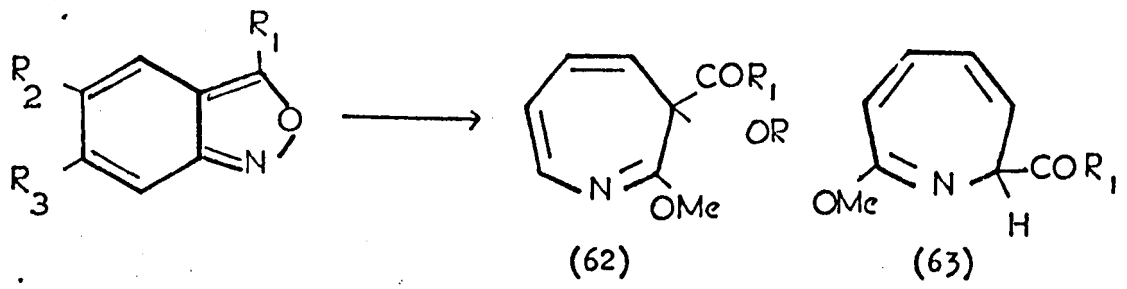


(61)

X = OMe or Cl

Later work by Ogata and his co-workers [50] showed that substituted azepines could be obtained by photolysing a series of substituted anthranils in methanol solutions. The azepines formed were either the 3H-isomer (62) or the 2H-isomer (63) as shown by Scheme 20.

SCHEME 20



(62) (63)

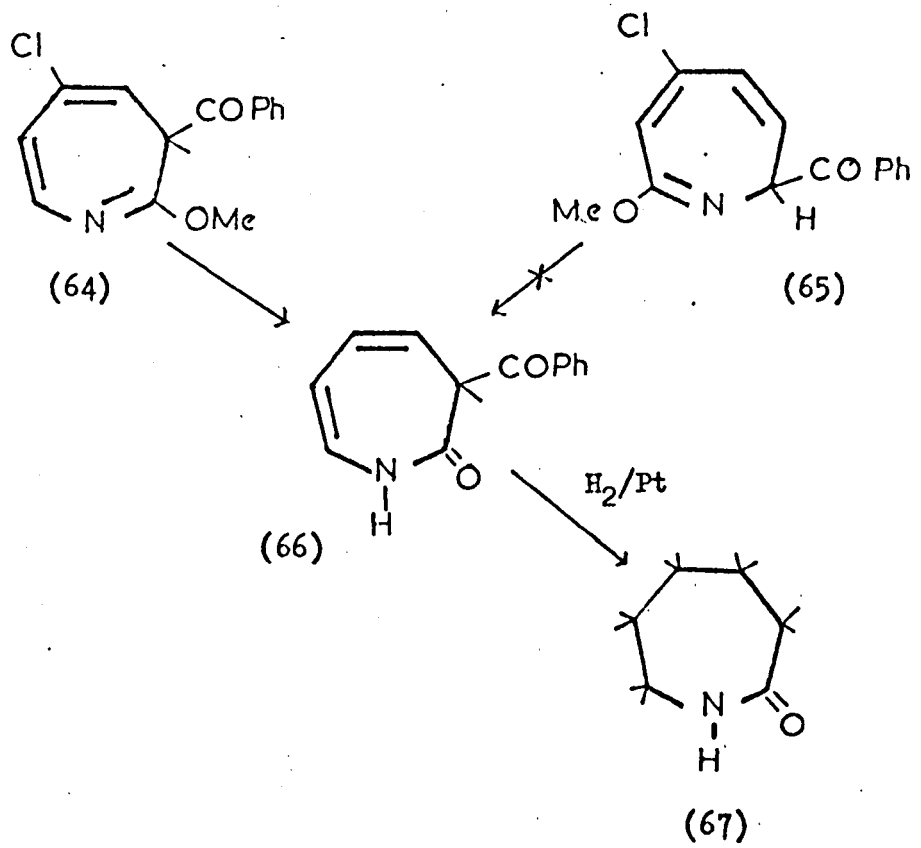
(a) R_1 = Ph R_2 = Cl R_3 = H

(b) R_1 = Me R_2 = R_3 = H

(c) R_1 = R_2 = H R_3 = Cl

^{1}H n.m.r. measurement indicated that the products were the 3H-isomers. This was confirmed by chemical degradation, since hydrolysis of the methoxy-azepines gave 5-chloro-2-oxo-3H-azepine (66) which on catalytic hydro-genation gave the dechlorohexahydro derivative (67). The 2H-isomer on hydrolysis would give 5-chloro-7-oxo-2H-azepine, which in fact was not obtained. The reactions are summarised in Scheme 21.

SCHEME 21

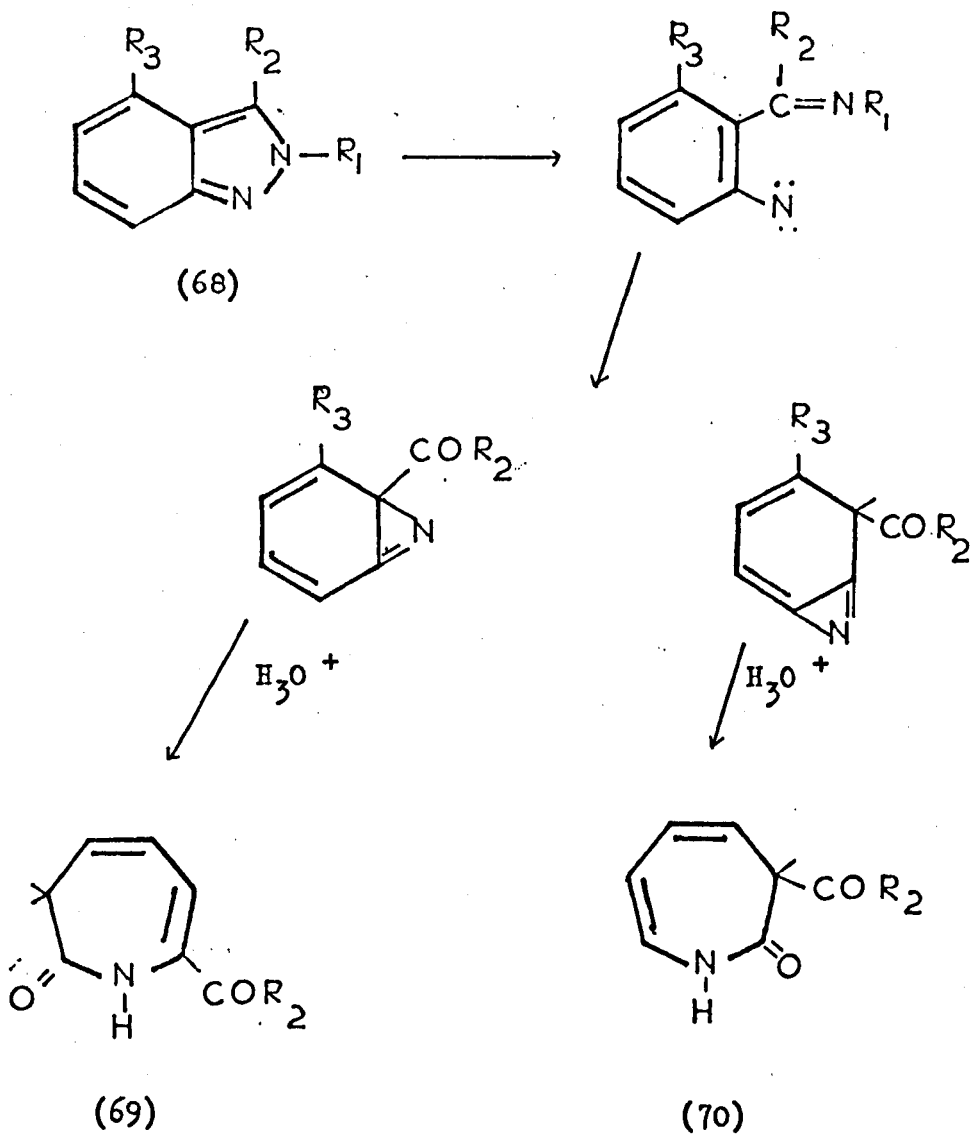


Analogous results were also obtained by Berwick [15] who obtained 3-acetyl-2-methoxy-3H-azepine (26) from 3-methylanthranil (25).

(ii) From Indazoles

Recently Heinzelmann and Maryy [51] have irradiated 2,3-dimethyl-indazole (68) in dilute sulphuric acid (pH=3.8) and have obtained 7-acetyl-1,3-dihydro-2H-azepin-2-one (69) and 3-acetyl-1,3-dihydro-2H-azepin-2-one (70). A nitrene mechanism is invoked to explain these results and the reaction is outlined in Scheme 22.

SCHEME 22



(68)

(69)

(70)

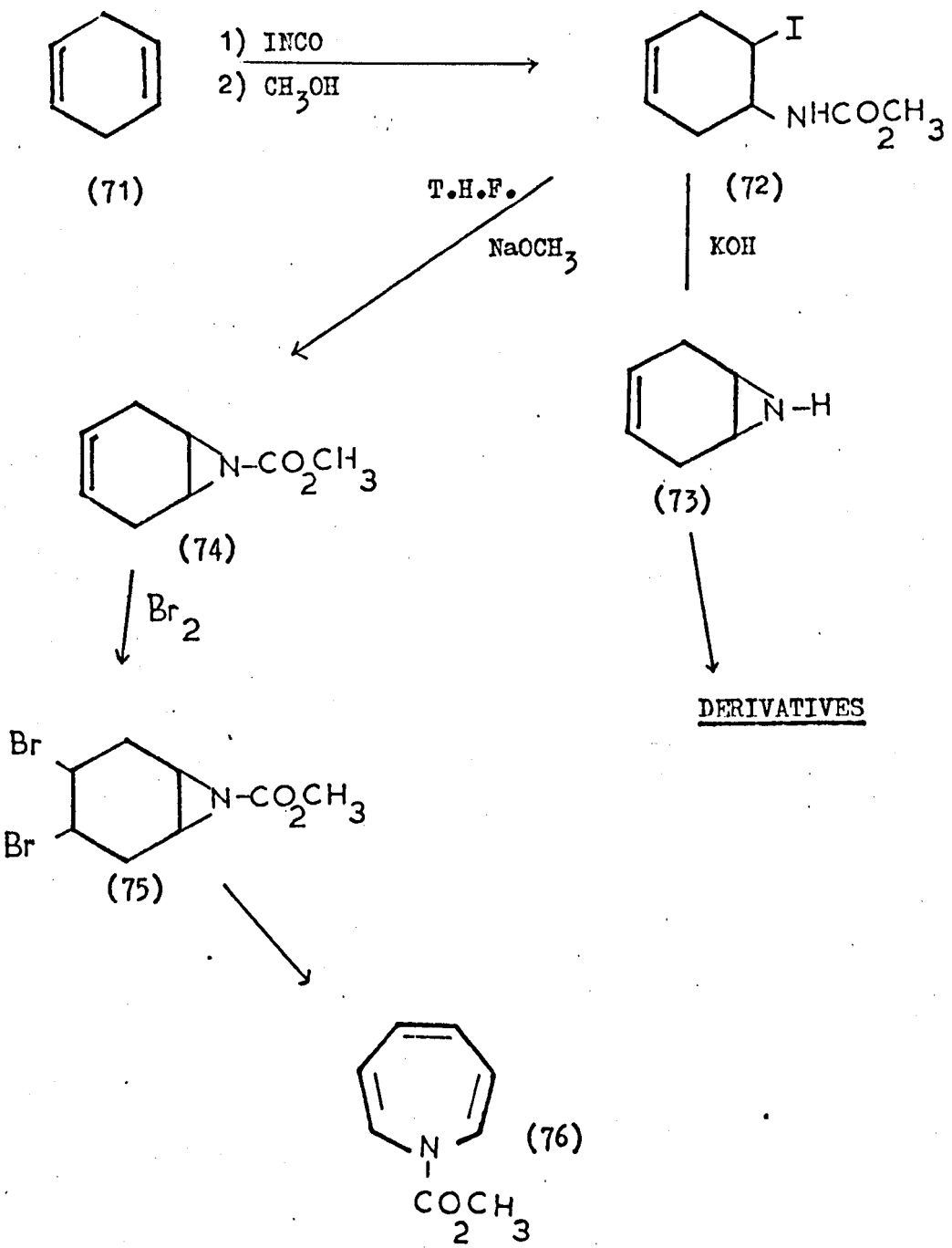
The results are in fact very similar to those observed by Berwick, [15] for the photolysis of 3-methylanthranil in piperidine. If the starting indazole ($R_3 = R_2 = H$ and $R_1 = CH_3$) is photolysed azepinones (69) and (70) are formed. With 3-methylanthranil in piperidine the products are 7-acetyl-2-piperidino-3H-azepine (30) and 3-acetyl-2-piperidino-3H-azepine (29). These on hydrolysis gives azepinones (69) and (70) respectively.

(iii) By Addition of Iodine Isocyanate to Double Bonds

One of the early difficulties in the formation of 1H-azepines, and to some degree the 3H-azepines, from azides, is that one is faced with the problem of isomers which are often very difficult to separate. A new approach to the synthesis of the 1H-azepines which avoided this problem was developed by Paquette, Kuhla, Barrett and Haluska [52] which gave only one isomer.

This method involved reacting iodine isocyanate [53,54,55] with 1,4 dihydrobenzene derivatives which are readily available by means of the Birch reduction of the appropriate aromatic compounds. 1,4-Cyclohexadiene (71) on treatment with silver cyanate and iodine in ether and then with methanol produced the crystalline iodocarbamate (72). Cyclisation of this carbamate with powdered sodium methoxide in dry tetrahydrofuran resulted in N-(methoxycarbonyl)aziridine (74) as outlined in Scheme 23.

SCHEME 23


1) INCO
2) CH3OH
I
NHCOCH3
(71)
(72)
T.H.F.
NaOCH3
KOH
N-H
(73)
N-CO2CH3
(74)
Br2
DERIVATIVES
Br
Br
N-CO2CH3
(75)
N
COCH3
(76)

Alternatively the carbamate (72) can react with aqueous potassium hydroxide to give the aziridine (73) which may be converted to a variety of derivatives by standard methods. Bromination of the aziridine (74) followed by dehydrobromination of (75) led to 1-(methoxycarbonyl)-1H-azepine (76) in good overall yield. Further studies [56,57,58,59] have shown that dihydrogenation of 1,2-aziridino-4,5-dibromocyclohexanes provide a simple scheme for synthesising many 1H-azepines and Table 8 gives some selective examples.

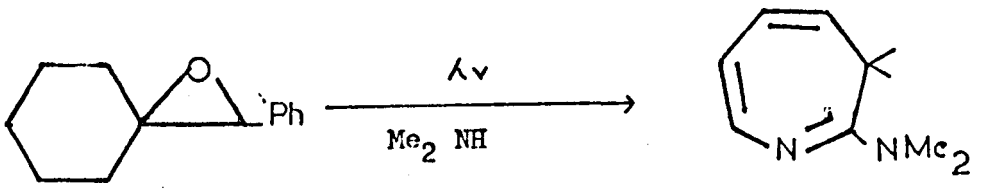
Table 8

1H-Azepines prepared by the Iodine Isocyanate Route

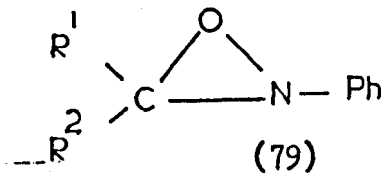
NITROGEN SUBSTITUENT	RING SUBSTITUENT	BPt or MPt(°C)	REF
$-COOCH_3$	-	59-61 (0.2 mm)	57
$-SO_2CH_3$	-	91-92	58
$-SO_2\ C_6H_5$	-	132-133	58
$-SO_2\ C_6H_4$ Br(p)	-	132.5-134	58
$-COO\ CH_3$	$2-CH_3$	62-64(0.1 mm)	56
$-COO\ CH_3$	$3-CH_3$	62-65(0.2 mm)	56
$-COO\ CH_3$	$4-CH_3$	62-65(0.2 mm)	56
$-SO_2\ C_6H_4$ Br(p)	$2-CH_3$	94-95	58
$-COO\ CH_3$	$2,7-(CH_3)_2$	55	59
$-COO\ CH_3$	$3,6-(CH_3)_2$	32	57
$-COO\ CH_3$	$4,5-(CH_3)_2$	61	59
$-COO\ CH_3$	$4,5-(CH_2)_4$	120 (0.05 mm)	58
$-SO_2\ C_6H_5$	$4,5-(CH_2)_4$	106	58

(iv) From Oxaziranes

Meyer and Griffin [60] obtained an azepine by irradiating the spirooxazirane (77) in freshly distilled dimethylamine. Once again the 3H-azepine was formed to the exclusion of other possible isomers.



Splitter and Calvin [61] also obtained small amounts of azepines from two phenyloxaziridines (79, R^1 R^2 as indicated).



(79)

(1) R^1 = p-$(CH_3)_2N$ C_6H_4 R^2 = H

(2) $R^1 = R^2$ = Ph

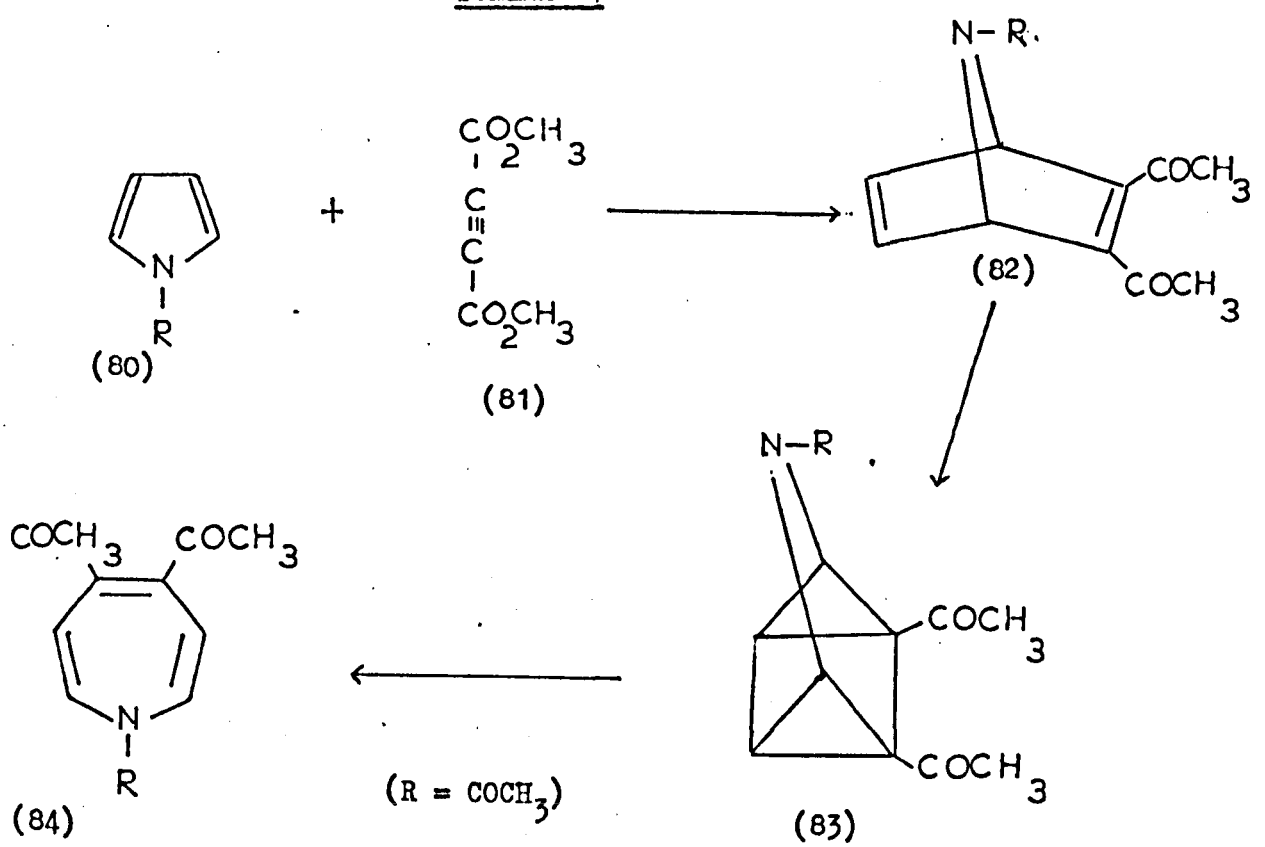
They postulated that the formation of the azepines is a reaction of the singlet nitrene formed by cleavage of the oxazirane ring. Photolysis of the two N-phenyloxaziridines disclosed competition between fragmentation leading to a phenyl nitrene and rearrangement leading to an anilide. Because fragmentation was somewhat hindered in the presence of molecular oxygen, an efficient triplet quencher, they deduced that fragmentation must arise through a triplet-state oxaziridine which lead to a triplet nitrene. Since aniline and

azobenzene are the main products and hardly any azepines are produced even in the presence of diethylamine, then the triplet-state phenyl nitrene could not be responsible for the formation of the azepines. This suggestion was backed up by the fact that phenyl azide in diethylamine in the presence of p-dimethylaminobenzaldehyde, a known triplet quencher, drastically reduces the yield of 3H-azepine (9), which would normally be quantitative without the triplet quencher, and increases the yield of aniline.

(v) From Pyrroles by Diels-Alder Reaction

Synthesis of the 1H-azepine (84) can also be accomplished by Diels-Alder addition of dimethylacetylene carboxylate [62] (81) to pyrrole derivatives (e.g. 80) substituted with a powerful electron withdrawing group (e.g. $COCH_3$) on the nitrogen. The synthesis is summarised in Scheme 24.

SCHEME 24

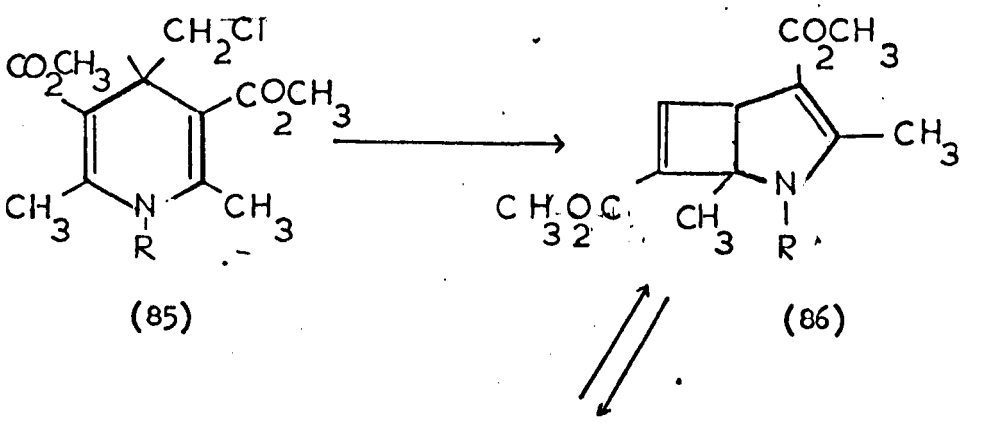


This method involves treating the pyrrole derivatives (80) with acetylenedicarboxylate (81) to give the Diels-Alder adduct (82) which on photolysis gives the thermally labile 3-azaquadricyclane (83) which then undergoes thermal rearrangement at 40°C to yield 4,5-disubstituted azepines (84) as shown in the reaction scheme.

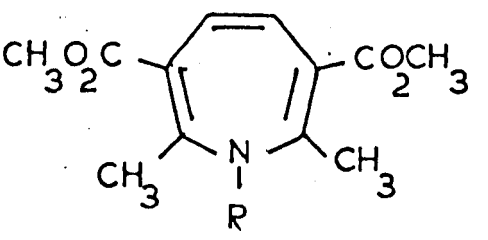
(vi) From Pyridine Derivatives

Johnson and Child [63,64] have shown that 4-(chloromethyl)-1,4-dihydro-1-methylpyridine (85) on treatment with potassium t-butoxide undergoes ring expansion to give 1,2,7-trimethyl-1H-azepine-3,6-dicarboxylate (87) (R = Me) or its valence tautomer dimethyl 1,2,3-trimethyl-2-azabicyclo {3,2.0} hepta-3,6-diene-4,7-dicarboxylate (86; R = Me) as shown in Scheme 25.

SCHEME 25



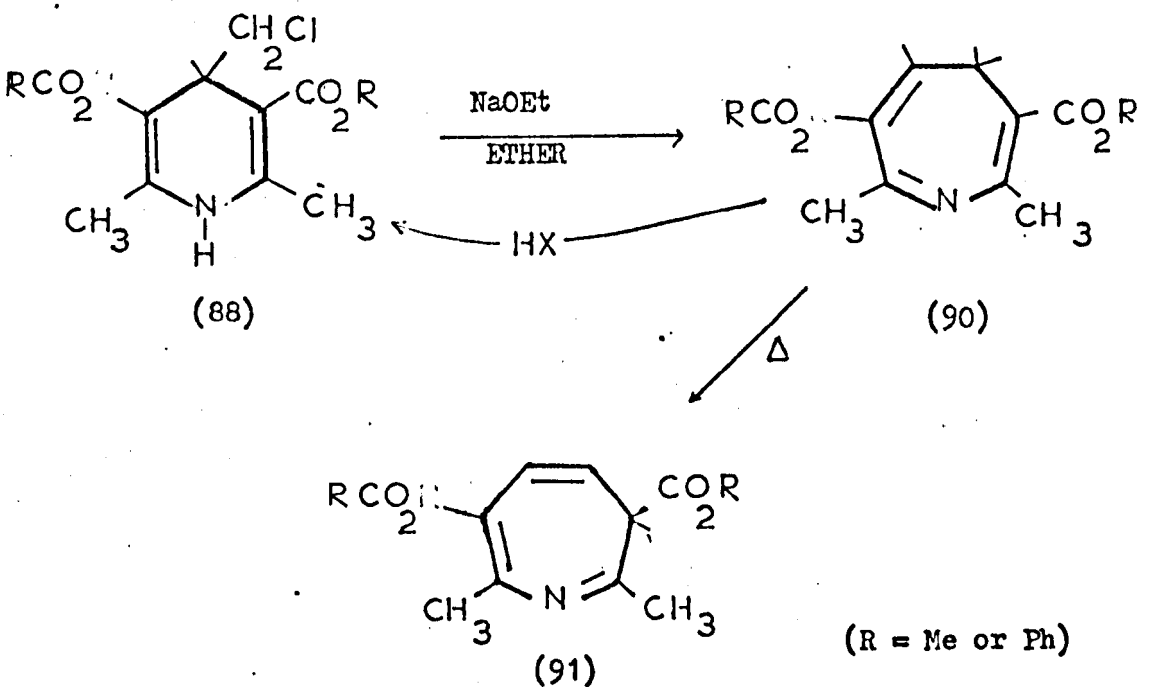
(85) (86)



(87) (R = CH_3)

Later work by Anderson and Johnson [65] showed that the esters of 4-(chloromethyl)-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylic acid (88) on treatment with sodium ethoxide undergoes ring expansion to give 4-ethoxy-4-5-dihydro-2,7-dimethylazepine-3,6-dicarboxylic esters (89; R = Me and Ph). These compounds readily lose ethanol to form derivatives of the 4H-azepine ring system (90) which on heating tautomerise to the 3H-azepine esters (91). These reactions are summarised in Scheme 26.

SCHEME 26



(88) (90) (91)

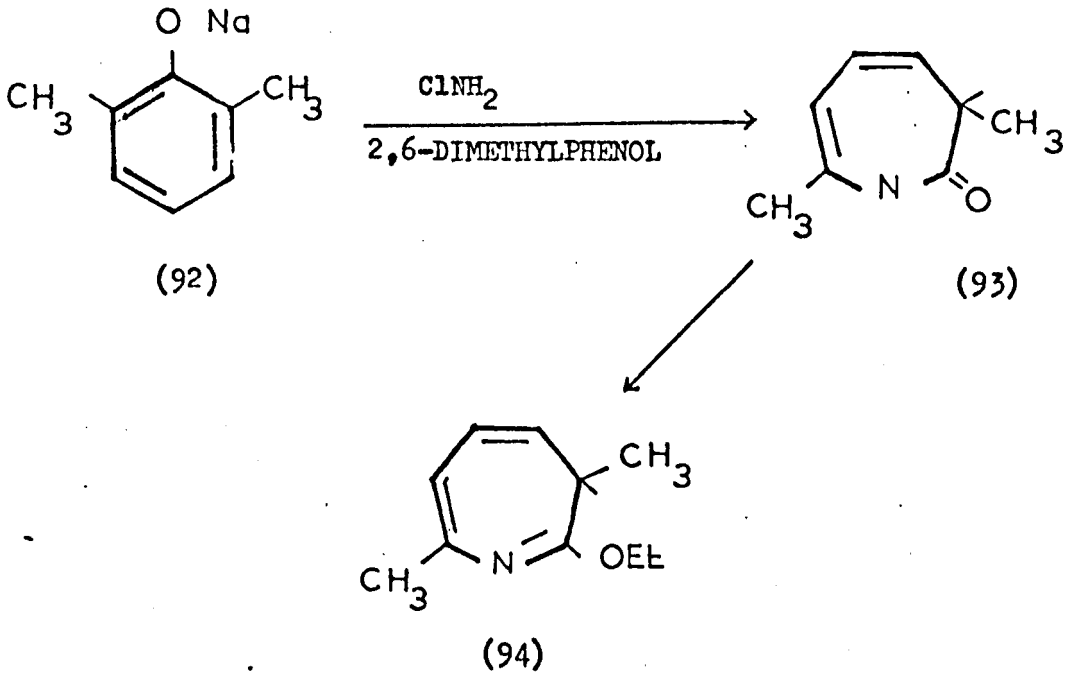
(R = Me or Ph)

The 4H-azepines (90) on treatment with hydrohalogen acids are converted back to the dihydropyridine (88).

(vii) From Phenols etc.

Phenoxide ions and chloramine have been employed in the synthesis of 3H-azepine derivatives. When hot solutions of sodio-2, 6-dialkyl- and 2,4,6-trialkyl phenoxides in excess of the corresponding phenols are treated with cold (-70°C) ethereal chloramine, 1,3-dihydro-2H-azepin-2-ones (93) are produced in good yields.[66,67,68,69] These azepinones on treatment with triethyloxonium fluoroborate yield 2-ethoxy-3H-azepines (94) as shown in Scheme 27.

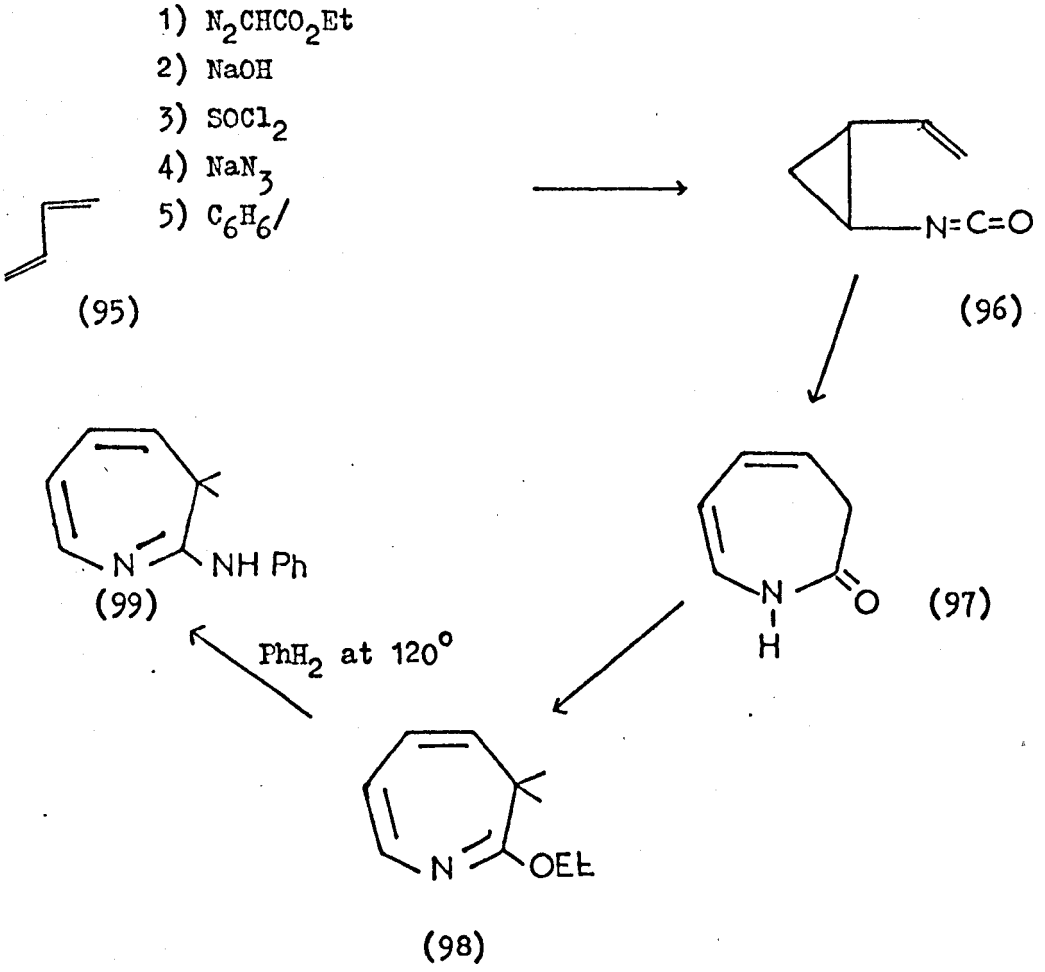
SCHEME 27



(92) (93) (94)

Vogel and co-workers[70,71] have reported a novel route to the synthesis of azepinones as outlined in Scheme 28.

SCHEME 28



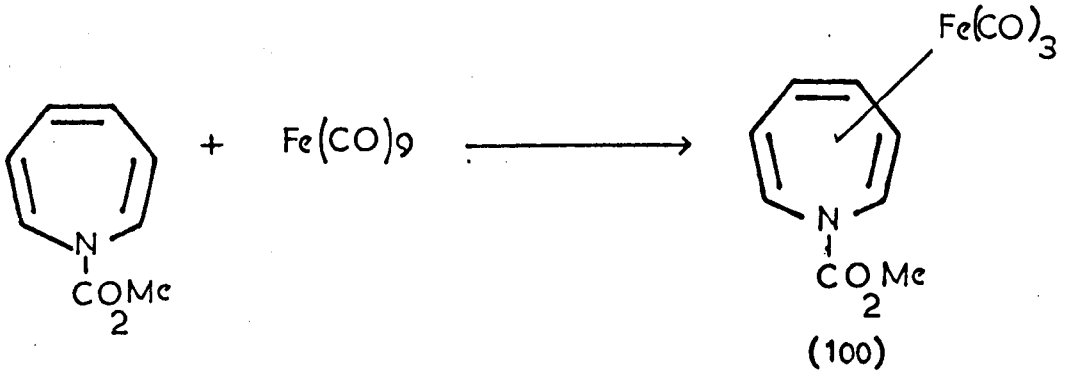
The diene is first treated with diazoethyl acetate to form a three-membered ring ester. The ester group is converted to the carboxylic acid with sodium hydroxide and then to the acid chloride with thionyl chloride. The chlorine is nucleophilically displaced by the azide group which on heating in dry benzene undergoes a Curtius rearrangement to give the isocyanate (96). This is then followed by ring expansion and cyclisation as shown in (Scheme 26) to give the azepinone (97). This azepinone was then converted to the 2-ethoxy-3H-azepine (98) using the oxonium fluoroborate reagent. The ethoxy ion is a good leaving group and can be replaced by, for example, aniline, to give 2-anilino-3H-azepine (6).

(viii) Other Methods

Transition metal complexes of 1H-azepines and Homo-1H-azepines have been reported.

The former [72] are synthesised by irradiation of N-methoxycarbonyl-1H-azepine (11) in tetrahydrofuran solution in the presence of iron pentacarbonyl, or by warming the 1H-azepine (11) with iron erreacarbonyl in cyclohexane solution. [73] The latter reaction is outlined in Scheme 29.

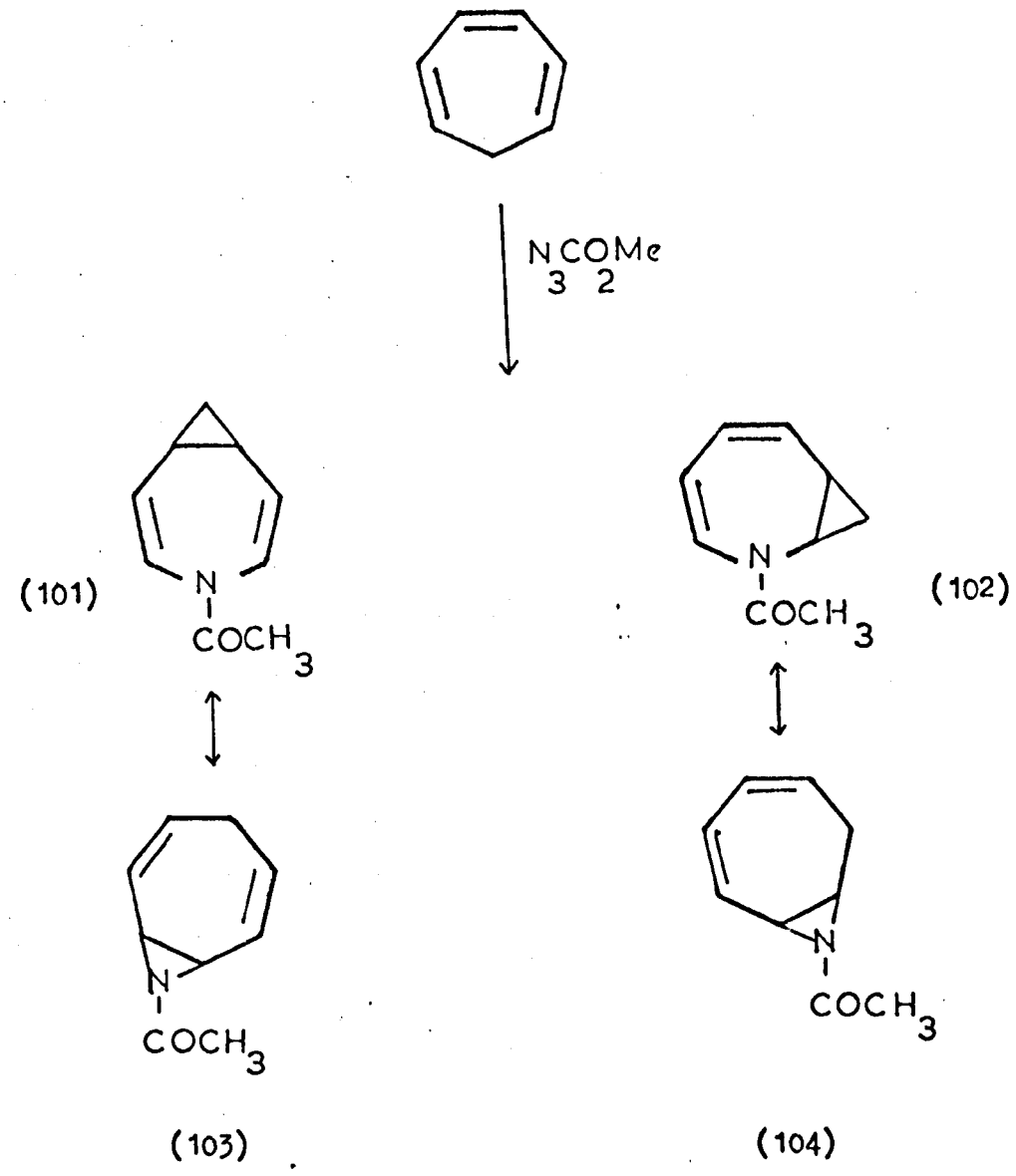
SCHEME 29



(100)

Homo-1H-azepines are made by treating an excess of cycloheptatriene with methyl azidoformate. This produces a mixture of 1:1 adducts from which a 35% yield of homo-azepines (103) and (104) can be isolated. [74] These products are presumably formed by valence tautomerisation of the initially produced aziridines (101) and (102) as indicated in Scheme 30.

SCHEME 30



Similar results have been obtained for the analogous ethyl azidoformate reaction.[75]

DISCUSSION

CHAPTER 2

Thermolysis and Photolysis of Aryl azides in Benzoyl Chloride

Aromatic azides can be broken down either photolytically or thermolytically to produce a reactive species called a nitrene. This may exist as a singlet (i.e. electron paired R-$\ddot{N}$) species or as the lower energy triplet (i.e. R-$\dot{N}\cdot$) diradical species. Chemical evidence for the intermediacy of both forms exists and their existence has been demonstrated using e.s.r. [76] and ultraviolet techniques. [77] The highly reactive nitrene once formed can stabilize itself in a number of ways namely:

(a) formation of an azo-compound [78]

(b) intermolecular hydrogen abstraction with ring closure [79]

(c) intermolecular hydrogen abstraction to yield an amine ($R-\dot{N}\cdot \rightarrow R-\dot{N}-H \rightarrow RNH_2$)

(d) the formation of an azirine intermediate which in the presence of certain nucleophiles undergoes ring expansion to form an azepine.

The formation of products from azide decompositions often depends on the nature of the solvent used for the decomposition. For example, amines [80] are usually obtained in solvents with a high availability of hydrogen, azobenzenes from inert solvents, and azepines from nucleophilic solvents e.g. diethylamine, aniline etc. Other solvents which have been used include acids and anhydrides. [81,82] Decomposition of aryl azides in acid solution [82] e.g. sulphuric or acetic acid yields p-aminophenols.

Smalley and Suschitzky [83] in this Research School thermolysed a series of substituted aryl azides in acetic anhydride and obtained amines, azobenzenes and acetylated o-aminophenols as shown in Table 1.

Table 1

Products of Decomposition of Aryl Azides in Boiling Acetic Anhydride

Azide RN_3	$2\text{-}NH_2.C_6H_3$(X, OH)		$RN{=}NR$	RNH_2
R	X	%	%	%
Ph	H	18.1	9.3	20.7
o-MeC_6H_4	3-Me	46	1.0	33
p-MeC_6H_4	5-Me	41.5	1.3	25
o-ClC_6H_4	3-Cl	21.8	4.5	19
p-$Br\text{-}C_6H_4$	5-Br	22.6	3.3	18
1-$C_{10}H_7$	—(1-$NH_2.C_{10}H_6$.OH-2)	20	4.3	28.5

The interesting feature of these decompositions was the formation of acetylated o-aminophenols. These products were rationalized as being formed by rearrangement of O,N-diacylphenylhydroxylamines, produced as intermediates in the reactions.

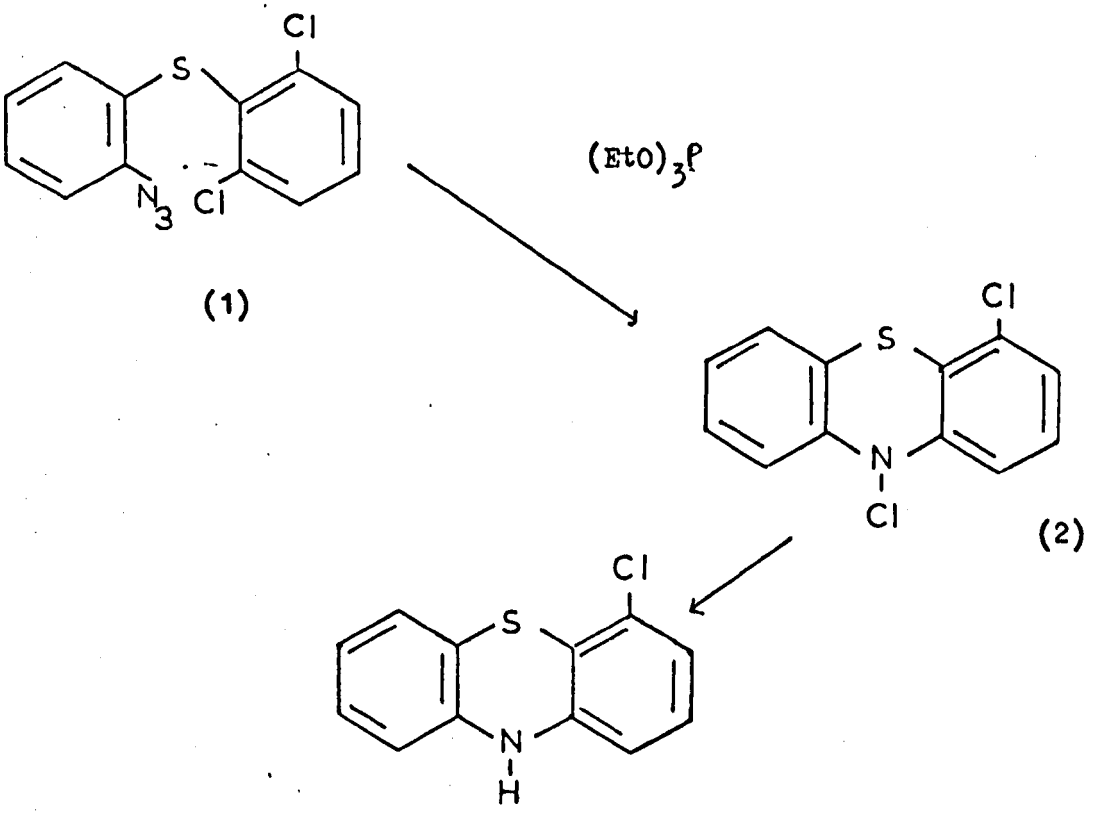
These results prompted us to investigate the decomposition of aryl azides in benzoyl chloride and the results of this investigation are reported in this chapter.

Acetyl chloride was first considered as a solvent but was rejected on account of its low boiling point (52°) which lies well

below the decomposition temperature of aryl azides. However, benzoyl chloride had an ideal boiling point (196°) for nitrene generation and was employed as the solvent. The aim of these decompositions was twofold:

(1) The acid chloride possesses a carbon-chlorine bond and, provided that a nitrene is formed in the decomposition, it could insert into the C-Cl bond leading to the formation of N-chloro compounds. This, in itself, is interesting since the only examples of nitrene insertion into a carbon-halogen bond have been reported by Suschitzky and his co-workers [84] and Cadogan and Kulik. [85] These latter workers used this idea to explain the formation of the dichlorophenothiazine (2) and monochlorophenothiazine (3) from the thermolysis of 2'-azidophenyl-2,6-dichlorophenylsulphide (1) in triethyl phosphite as shown in Scheme 1.

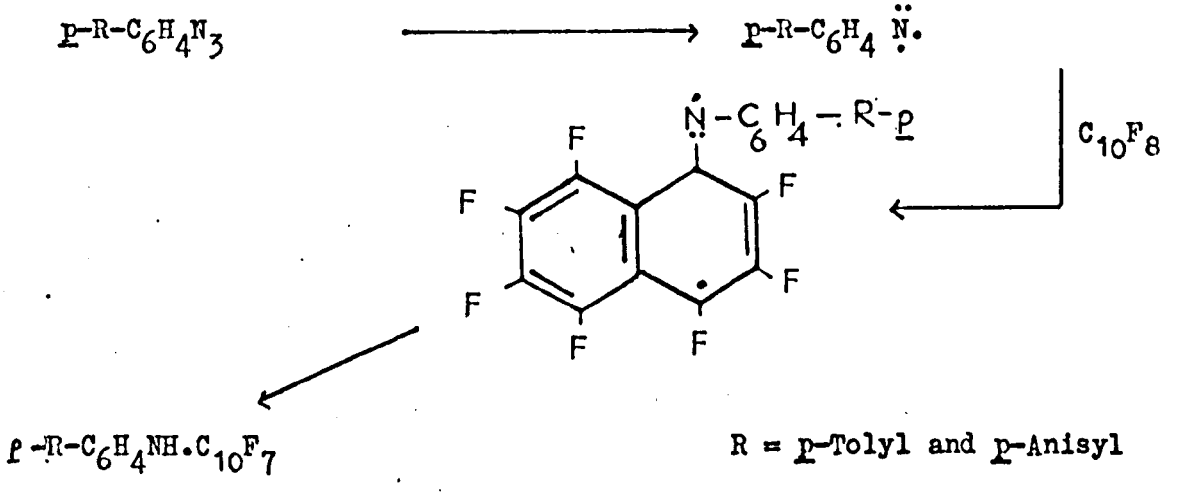
SCHEME 1



(1) (2) (3)

Suschitzky and his co-workers [84] showed that aryl nitrenes will insert into the C-F bond of pentafluoronaphthalene to give the corresponding N-aryl-1-heptafluoronaphthylamines (4) as shown in Scheme 2.

SCHEME 2



(2) N-chloro compounds at elevated temperatures are known to undergo an Orton type rearrangement and hence these reactions would be an ideal synthesis for chloro-substituted benzanilides.

Preparation of Aryl Azides and Benzoyl Chloride

(a) Aryl azides

The required aryl azides were prepared by the Smith and Brown method. [86] This involved diazotisation of the respective amines followed by treatment of the resulting diazonium solutions with sodium azide - sodium acetate mixture. The azides so formed were then extracted with ether and washed with 10% sodium bicarbonate and 5% sodium hydroxide solutions, to remove acidic impurities, and finally with water. The ethereal extracts were then dried over

anhydrous magnesium sulphate and the azides were purified by chromatography on an alumina column. The following azides were prepared by this method, phenyl-(5), p-methylphenyl-(6), p-methoxyphenyl-(7), o-methoxyphenyl-(8), o-nitrophenyl-(9), p-nitrophenyl-(10), p-chlorophenyl-(11), and 2-azidobiphenyl-(12).

(b) Benzoyl Chloride

Commercial benzoyl chloride was freed of hydrogen chloride by Oakwood and Weisgerber's method [87] i.e. the acid chloride in benzene solution was washed with 10% sodium bicarbonate solution then dried over anhydrous magnesium sulphate. Fractional distillation of the mixture removed the benzene and gave pure benzoyl chloride (b.p. 196°) which was then stored in a dark bottle over anhydrous potassium carbonate.

(c) Methods of Decomposition of Aryl Azides

Two methods of decomposition were employed. The first involved heating under reflux a 10% solution of azide in benzoyl chloride at 150° until all the azide had disappeared (Method 1). This was confirmed by thin layer chromatography and infrared techniques. The second method which applied to those azides which were liquids, with the exception of o-methoxyphenyl azide (8), involved adding an azide-acid chloride mixture to an excess of benzoyl chloride maintained at 160°. The mixture was then heated under reflux for one hour (Method 2). In both methods, the reactions were carried out under nitrogen, and when the thermolyses were complete the excess of acid chloride was removed by vacuum distillation and in most cases a tarry mass was left behind.

(d) Identification and Confirmation of Structure of Products

In view of the fact that it was impossible to remove all the benzoyl chloride from the reaction mixture, and that during some stage in the separation of the products the acid chloride would be hydrolysed to benzoic acid, the tarry materials were preabsorbed onto alumina and then separated by column chromatography. The products separated from the decompositions using Method 1, are summarised in Table 2.

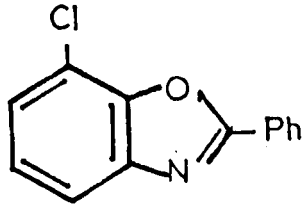
Table 2

Decomposition products of Aryl azides in Benzoyl Chloride

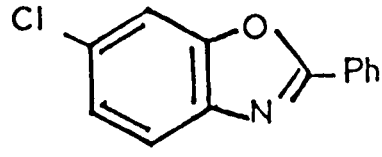
Aryl Azide	Product	Yield %
H	6-chloro-2-phenylbenzoxazole	2
	azobenzene	2
	o-chlorobenzanilide	11
	Benzanilide	50
p-Me	4,4'-dimethylazobenzene	2
	N-benzoyl-2-chloro-4-methylaniline	19
	N-benzoyl-4-methylaniline	34
o-MeO	N-benzoyl-2-chloro-6-methoxyaniline	55
p-MeO	4,4'-dimethoxyazobenzene	6
	N-benzoyl-2-chloro-4-methoxyaniline	67
p-NO_2	Polymeric materials	-
o-NO_2	Benzofuroxan	83
p-Cl	4,4'-dichloroazobenzene	15
	N-benzoyl-4-chloroaniline	15
Biphenyl	N-benzoylcarbazole	10
	Carbazole	75

(i) Decomposition of Phenyl Azide

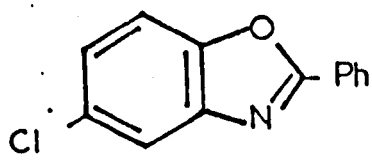
The first product obtained from the alumina column on eluting with light petroleum (b.p. 40-60°) was a white solid (m.p. = 98°). Analytical data indicated that this solid had a molecular formula $C_{13}H_8ClNO$ which was confirmed by mass spectrometry, which indicated a molecular ion peak at M^+, 229. The presence of chlorine was further confirmed by the Beilstein copper wire test, and an initial loss in the mass spectrum of 35 units from the parent mass ion. Infrared evidence confirmed the absence of NH and C=O groups but indicated a (C=N) at 1620 cm^{-1}. This evidence suggested a benzoxazole system [88] and the compound could have any one of the following structures:



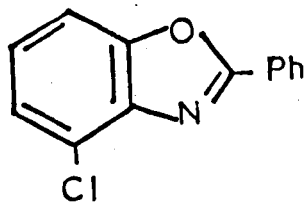
(13)



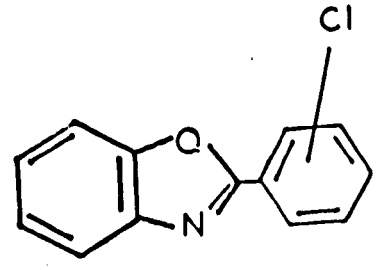
(14)



(15)



(16)



(17)

A literature survey showed that only the 6-chloro-2-phenyl-, and the 5-chloro-2-phenyl isomers were known, and both had melting points close to the azide decomposition product. Hence 5-chloro- (15) and 6-chloro-2-phenylbenzoxazole (14) were synthesised by the methods outlined below.

The first involved [89] heating a mixture of 2-benzamido-5-chlorophenol with phosphorus pentoxide at 230°; whereupon cyclisation to the required benzoxazole was observed. The second synthesis employed a method developed by Suschitzky and his co-workers [90] who showed that p-substituted aromatic azides on thermolysis in a mixture of polyphosphoric acid and benzoic acid gave rise to the corresponding 6-substituted benzoxazole. Thus heating p-chlorophenyl azide (11) with a mixture of polyphosphoric acid and benzoic acid led to the chlorobenzoxazole (14) (m.p. = 98-99°) which was identical to the product made by the alternative method. 5-chloro-2-phenylbenzoxazole (15) (m.p. = 102°) was also synthesised [91] by heating 2-hydroxy-4-chloroaniline with benzoic acid and polyphosphoric acid. Comparison of the infrared spectrum of the 6-chloro isomer with that of the reaction product, together with a mixed melting point (m.p. = 98°), indicated that the benzoxazole was in fact the 6-chloro-2-phenyl isomer.

Further elution of the column with light petroleum (b.p. = 40-60°) gave an orange solid which was suspected to be azobenzene (18). This was confirmed by comparison of infrared spectra and mixed melting point (m.p. = 68°) with the reaction sample and an authentic sample of azobenzene.

Continued elution of the column with benzene gave a white solid (m.p. = 88°). It gave a positive Beilstein copper wire test

PhN=NPh
(18)

o-ClC$_6$H$_4$NHCOPh
(19)

and showed ν(NH) 3240 cm^{-1} and ν(C=O) 1660 cm^{-1} in the infrared spectrum. This compound appeared to be an amide and was possibly ortho or para chlorobenzanilide. Both isomers were unambiguously synthesised by benzoylation of o-chloroaniline and p-chloroaniline respectively. Mixed melting point (m.p. = 87°) with the reaction sample (m.p. = 87°) confirmed that the reaction product was o-chlorobenzanilide (19) rather than the p-chloro isomer.

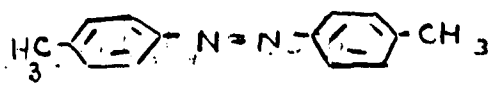
The final product to be obtained from the column was a white flaky solid (m.p. = 162°). Infrared data indicated that this compound was an amide, ν(NH) 3350 cm^{-1} and ν(C=O) 1660 cm^{-1} and a negative Beilstein copper wire test showed the absence of chlorine. This compound was suspected to be benzanilide (20) and this was confirmed by mixed melting point (m.p. = 161°) with an authentic sample.

When the alternative method of decomposition, i.e. Method 2, was employed only two products namely azobenzene (18) and benzanilide (20) were isolated from the reaction mixture. The reason for this difference in reaction products is not clear.

(ii) Decomposition of p-Methylphenyl azide

Like the previous decomposition an orange solid (m.p. = 143°) was obtained on eluting the alumina column with light petroleum (b.p. = 40-60°), which was suspected to be 4,4'-dimethylazobenzene (21). Unambiguous synthesis of this azo compound was accomplished by oxidising [89] p-toluidine with benzoyl peroxide in benzene solution. Comparison of the infrared spectra and mixed melting point of the reaction and synthetic products (m.p. = 143°) proved the structure to be the azo compound (21).

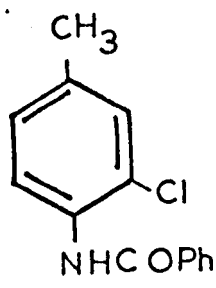
$C_6H_5NHCOPh$ (20)


(21)

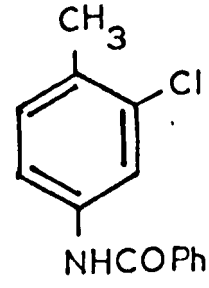
The next product to be obtained was a white crystalline solid (m.p. = 138°).

The mass spectra data showed a molecular ion at 245 mass units with fragmentation losses of 35 and 108 units respectively, corresponding to loss of Cl and PhCO.

Elemental analysis indicated that the compound had a molecular formula $C_{14}H_{12}ClNO$, while infrared data, ν(NH) 3260 cm^{-1}; ν(C=O) 1650 cm^{-1} suggested that the compound was an anilide. From the evidence obtained, the product was considered to be either the 2-chloroanilide (22) or its 3-chloro isomer (23).



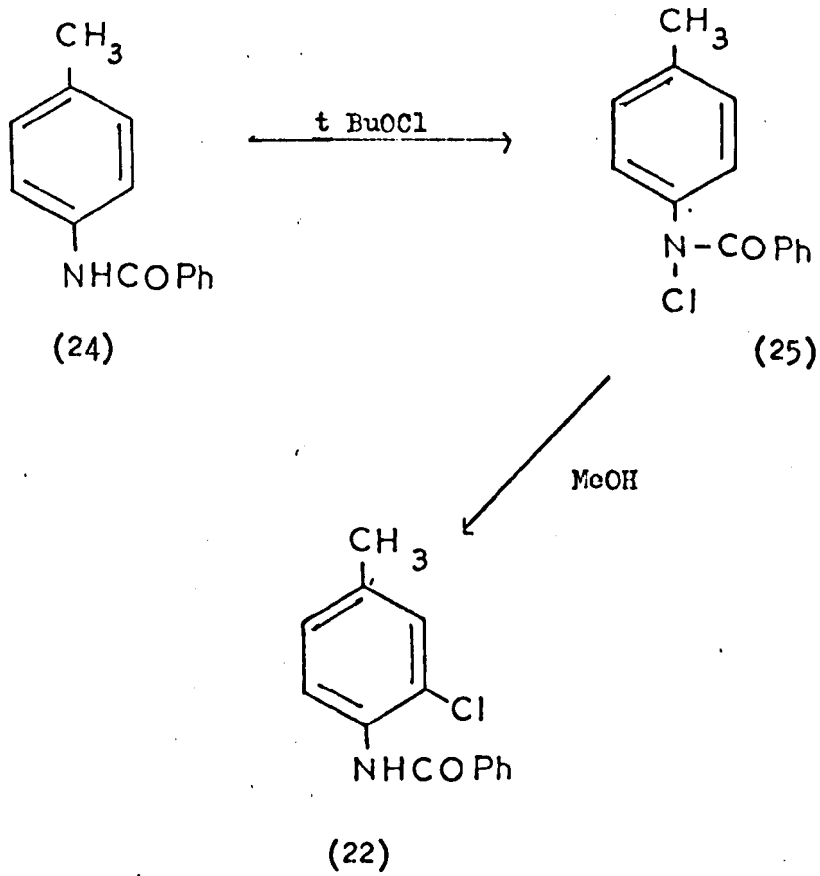
(22)



(23)

N-benzoyl-3-chloro-4-methylaniline (23) (m.p. = 119°) was synthesised by benzoylation of 3-chloro-4-methylaniline under Schotten - Baumann conditions, and gave a depressed mixed melting point with the azide decomposition product. Also the infra-red spectra ν(NH) 3320 cm^{-1} and ν(C=O) 1655 cm^{-1}, was non-superimposable with the infrared spectrum of the reaction product. The isomeric 2-chloro-anilide (22) was synthesised [92] by treating N-benzoyl-p-toluidine (24) with t-butyl hypochlorite in methanol containing a quantity of borax solution, whereupon the N-chloro-N-benzoyl-p-toluidine (25) was obtained. This product on heating under reflux in methanol for 2 hours rearranged to give the 2-chloroanilide (m.p. = 138°). This product was found to be identical (mixed melting point and superimposable infrared spectra) to that of the reaction product.

SCHEME 3



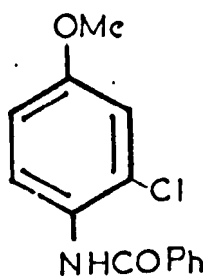
Continued elution of the column gave a third product (m.p. = 156°) whose infrared spectrum once again showed it to be an amide ν(NH) 3320 cm^{-1} and ν(C=O) 1660 cm^{-1}. This compound was suspected to be the anilide (24) and this was confirmed by mixed melting point (m.p. = 156°) with a sample of N-benzoyl-p-toluidine.

Like the previous decomposition, i.e. that of phenyl azide (Method 2), dropping the azide-acid chloride mixture into hot acid chloride increased the yields of the azo compound (21) from 2% to 4% and the anilide (24) from 34% to 45% but decreased the yield of the chlorinated anilide (22) from 19% to 12%.

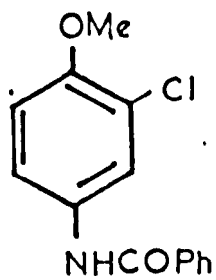
(iii) Decomposition of p-Methoxyphenyl Azide

As with the previous decompositions, the first product to be obtained from the alumina column on eluting with light petroleum (b.p. = 40-60°) was the azo compound, 4,4'-dimethoxyazobenzene (26) (m.p. = 164°). This structure was confirmed by an unambiguous synthesis [78] of the azo-compound (26) formed by thermolysing p-methoxyphenyl azide in cumene.

The second and final product obtained from the column by eluting with a mixture of benzene and ether was a white solid, (m.p. = 169-170°). Mass spectral evidence showed the molecular ion to be 261^+ with once again fragmentation losses of 35 and 105 units respectively corresponding to the loss of chloro and benzoyl groups. An infrared spectrum showed ν(NH) 3260 cm^{-1} and ν(C=O) 1655 cm^{-1}, indicating that the structure was once again an anilide, and as previously, the product could be either one of the two isomeric anilides (27) or (28).

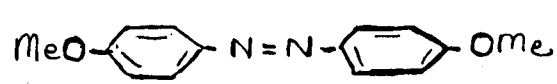


(27)



(28)

The chloroanilide (28) was synthesised by benzoylation of 3-chloro-4-methoxyaniline. The product obtained after recrystallisation (m.p. = 140°) had a non-superimposable infrared spectrum with the azide decomposition product, and also showed a depression of the melting point. This proved its non-identity with the anilide from the azide thermolysis. Synthesis of the 2-chloro-4-methoxy isomer (27) was not accomplished via the N-chloro compound as attempts to



(26)

synthesise this proved unsuccessful. However, the isomer (27) was obtained by benzoylation of 2-chloro-4-methoxyaniline. This product (m.p. = 169°) proved to be identical with the reaction product and confirmed that the azide decomposition product was N-benzoyl-2-chloro-4-methoxyaniline (27).

(iv) Decomposition of p-Nitrophenyl Azide

Despite careful thin layer chromatographic investigation of the reaction mixture, only polymeric materials were obtained from the decomposition of p-nitrophenyl azide in benzoyl chloride.

(v) Decomposition of o-Nitrophenyl Azide

Unlike previous decompositions no azo compound was isolated. Instead chromatographic separation of the reaction products yielded a pale yellow solid (m.p. = 71°), the mass spectrum of which showed a molecular ion of 136 units. The mass spectrum also indicated an initial loss of 16 mass units, features characteristic of some N-oxides. This was supported by infrared evidence which showed a peak at 1200 cm^{-1} characteristic of N-oxides, together with two peaks at 1605 cm^{-1} and 1630 cm^{-1}, features indicative of two (C=N) groups.

From this evidence a furoxan system [93] was suspected and the product was thought to be benzofuroxan (29).

This was confirmed by heating the azide (9) under reflux in xylene [94] whereupon benzofuroxan (29) was obtained, whose infrared spectrum was superimposible with the reaction product. The interesting feature about the decomposition of this azide (9) is that the same product is formed irrespective of which solvent is employed, and this low temperature decomposition usually implies that the decomposition is assisted. This point will be discussed further in this and in following chapters.

(vi) Decomposition of p-Chlorophenyl Azide

Like most of the previous decompositions an orange solid (m.p. = 188°) was the first product to be obtained from the alumina column. This, was thought to be 4,4'-dichloroazobenzene (30) and was confirmed by mixed melting point (m.p. = 187°) determination with an available sample of the suspected azo compound.

The second product to be obtained was a white solid (m.p. = 192°). Mass spectral evidence showed the molecular ion to be 231^+ with, as before, fragmentation losses of 35 and 105 units respectively.

Infrared evidence ν(NH) 3240 cm^{-1} and ν(C=O) 1655 cm^{-1} indicated that the compound was an anilide. This compound was suspected to be 4-chlorobenzanilide (31) and this in fact was confirmed to be so by comparing the reaction product with a sample of 4-chlorobenzanilide made by benzoylating 4-chloroaniline.

Since this azide was a liquid, the alternative method (Method 2) was carried out and the yields of the azo compound (30) and the chlorinated anilide (31) were found to be virtually identical. However the interesting feature which arose from this azide decomposition was that no dichlorinated anilide was formed irrespective of which method of decomposition was employed.

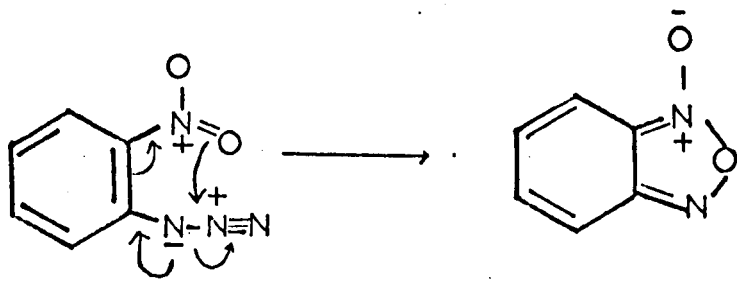
(vii) Decomposition of 2-Azidobiphenyl

Previous decompositions of this azide in various solvents [79] have shown that in general carbazole (32) is formed in high yield.

Decomposition of this azide in benzoyl chloride was no exception in that carbazole (32) (m.p. = 238°) was obtained. However another product was isolated by chromatography which melted at 98°. Its infrared spectrum showed the absence of NH but a carbonyl absorption at 1685 cm^{-1} was present. This compound was suspected to be N-benzoylcarbazole (33) (m.p. = 98°) and was thought to have arisen by the benzoylation of preformed carbazole. An authentic sample of N-benzoylcarbazole was prepared by benzoylating carbazole and the infrared spectrum of the product was superimposable with that of the azide decomposition product.

(e) Discussion of Results

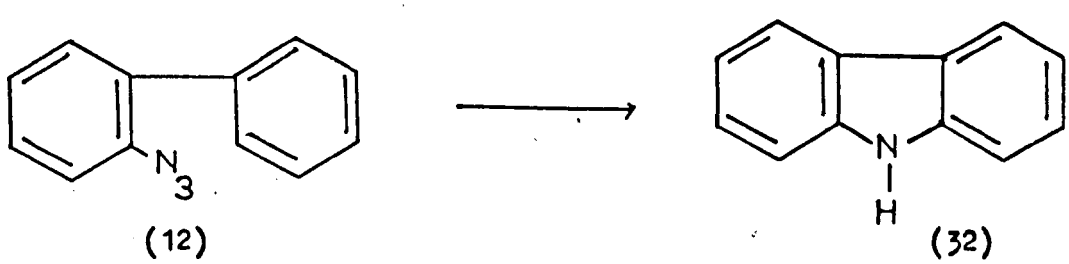
As expected o-nitrophenyl azide and o-azidobiphenyl yield benzofuroxan (29) and carbazole (32) respectively. In the former case, it has been shown by kinetic measurements [95] that this reaction proceeds by a neighbouring group displacement of the nitrogen from the azide by the nitro substituent rather than by a nitrene mechanism.



(29)

Smith and his co-workers [79] have shown that carbazole (32) arises via formation of a nitrene which intramolecularly abstracts hydrogen from the adjacent phenyl ring with subsequent ring closure as shown in Scheme 4.

SCHEME 4



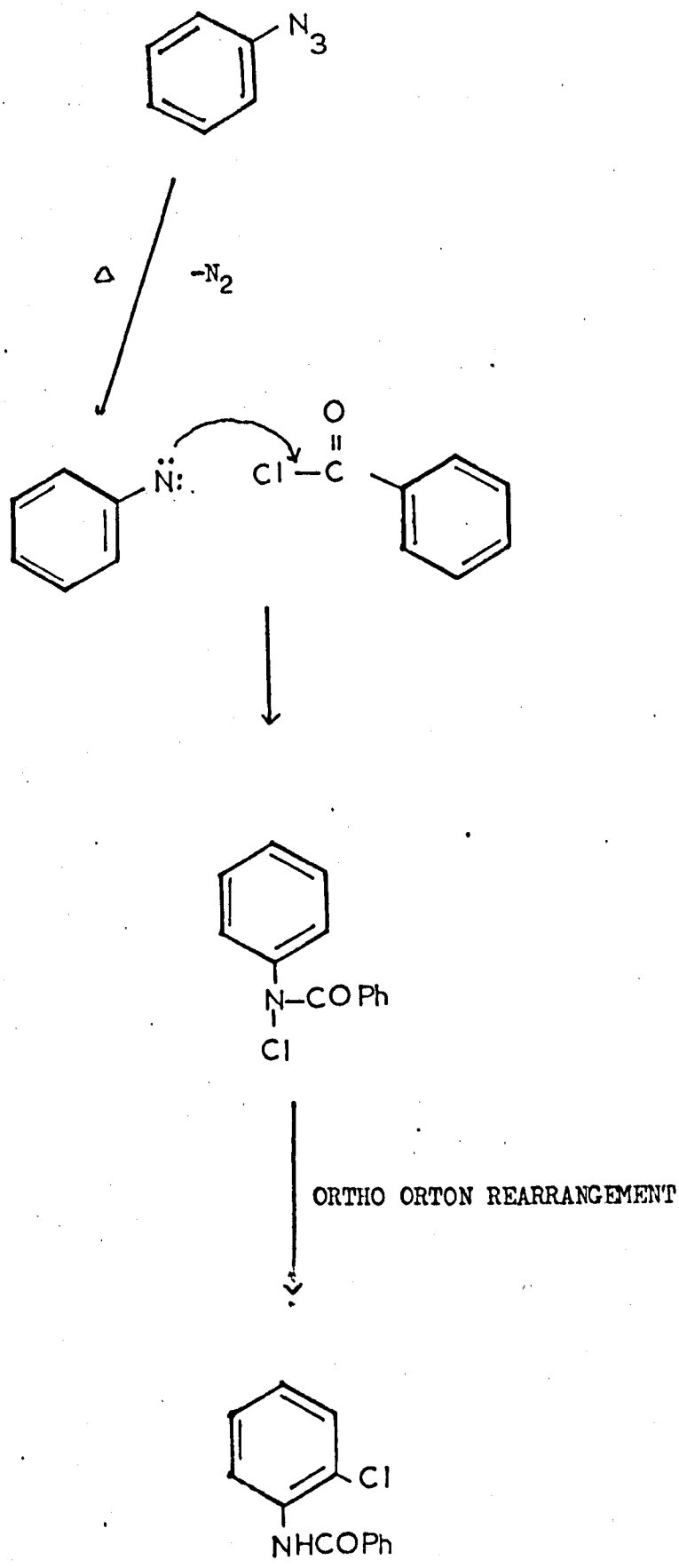
(12) (32)

In fact a nitrene involvement in this reaction was later confirmed by Dyall and Kemp [96] who showed that the phenyl group ortho to the azido function does not involve any anchimeric assistance and that the decomposition of this azide (12) proceeds via a nitrene.

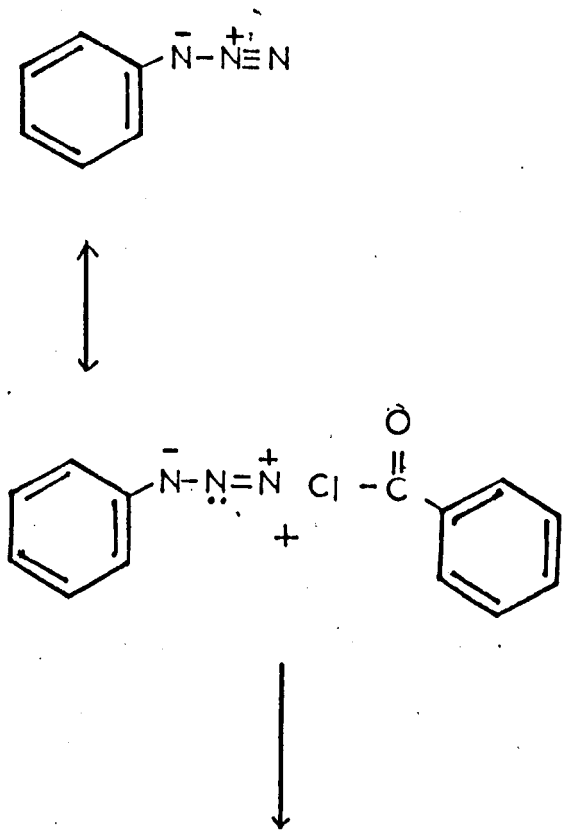
With p-nitrophenyl azide, only polymeric materials were obtained and this is in accord with previous work by Smalley and Suschitzky [83] who obtained only tars from the decomposition of this azide (12) in acetic anhydride.

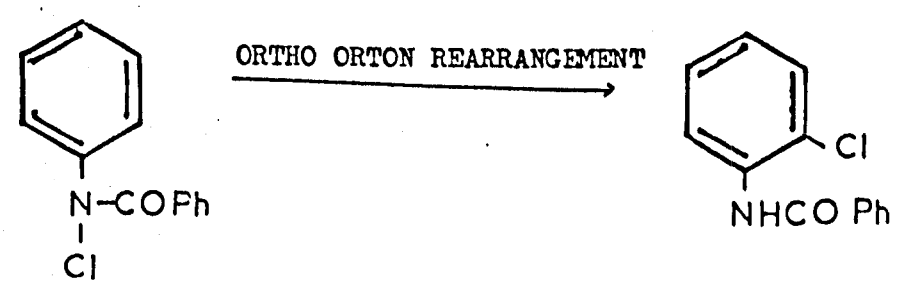
In the case of the other substituted aryl azides, azo-compounds, benzanilides and chlorobenzanilides are formed. Both these former products can be rationalised in terms of a triplet nitrene, which will be discussed later. However, less obvious is the mode of formation of o-chlorinated anilides in the case of phenyl; p-methylphenyl and p-methoxyphenyl azides. If a nitrene is involved, it could insert into the carbon-halogen bond of the acyl halide leading to the formation of an N-chlorobenzanilide, which at such temperatures would undergo an ortho Orton type rearrangement. [97] Alternatively, a triazoline type intermediate could be formed by the addition of the azide to the C=O of the acyl halide. Loss of nitrogen followed by intermolecular chloride ion migration would lead to the N-chloro compound which could then undergo the ortho Orton type rearrangement. These pathways are summarised in Schemes 5 and 6 respectively.

SCHEME 5



SCHEME 6


N-N≡N
N-N=N
Cl
C
O
+
Cl
Ph
N
N
N
O


N-COPh
Cl
ORTHO ORTON REARRANGEMENT
Cl
NHCO Ph

To show which of these schemes, if any, might be favoured, kinetic studies had to be employed. However, one of the main drawbacks in kinetic studies, which are based on the evolution of nitrogen from an azide decomposition is that the reaction may involve either a nitrene or triazoline intermediate. In both cases nitrogen is evolved and it is tedious to distinguish between the two processes. However, Hall and his co-workers [19] have shown that these pathways can be distinguished by calculating the activation energy of decompositions which are thought to be assisted i.e. o-azidobenzophenones with large negative (- 6 - 21 cal deg^{-1} mol^{-1}) and comparing this with values from reactions which are known to involve a nitrene mechanism i.e. values [98] obtained from the addition of phenyl azide to olefines (-30 - 35 cal deg^{-1} mol^{-1}). Because of this large difference in entropy values of the o-azidobenzophenones, these workers [19] were able to postulate that the decompositions of these azidoketones are assisted and probably occurs via a 1.3 dipolar addition.

Because of these minor difficulties we decided to use the method of independence of the rate on the nature of the solvent. This method is well documented [99,100,101] and involves the rate of disappearance of the nitrene or its precursor and is not based on the evolution of nitrogen. A nitrene mechanism demands that the rate should vary very little with changes in solvent since the latter is presumed to participate in the transition state only by solvation. This method also has one advantage over the nitrogen evolution method in that rapid disappearance of the precursor, in particular at a low temperature, often gives an indication that the reaction is not proceeding via a nitrene mechanism.

We therefore carried out the following reactions.

(a) Thermolysis of p-methylphenyl azide (0.1 mol) in bromobenzene (50 ml) at 145°C.

(b) Thermolysis of the same azide (0.1 mol) in the presence of benzoyl chloride (0.1 mol) in a mixture made up to a total volume of 50 ml with bromobenzene.

Extracts were taken from the mixtures at various intervals and infrared spectra were run on the aliquots. The azide peaks at 2140 cm^{-1} were carefully cut out from the paper and weighed.

Some standards were also prepared by taking the infrared of azide solutions of known concentrations, cutting out the azide peaks from the paper, and then weighing the respective cuttings.

From these standards the respective concentration of azide at any particular time in the reaction could be worked out. The log of the azide concentrations were then plotted against the respective times as shown in Tables 2 and 3. (See following pages).

The rate constants obtained from the two reactions were:

$$K_1 = 1.1 \times 10^{-4} \text{ sec}^{-1}$$

$$K_2 = 1.05 \times 10^{-4} \text{ sec}^{-1}$$

From these results, it was concluded that the acid chloride is not participating in the rate determining step of the reaction and that a nitrene mechanism is possible. Hence Scheme 5 i.e. the 1,3-dipolar addition can be eliminated. However, we realize that errors may arise in this method owing to the non-uniformity of the infrared paper. Nevertheless we feel that such errors are slight and will not significantly affect the rate observed.

Table 2

Tolylazide in Bromobenzene

STANDARDS

SCJ	WEIGHTS
0.2	0.990
0.16	0.880
0.12	0.0752
0.18	0.0564
0.04	0.0318
0.02	0.0170

This is the calibration of concentration/weights from which we can obtain log c.

Time	Weights	SCJ	Log of Con.(c)
0	0.0964	0.19	-
30	0.1066	-	-
60	0.0978	0.198	0.3
90	0.0905	0.168	0.255
120	0.0790	0.130	0.114
150	0.0712	0.110	0.045
180	0.0623	0.091	0.959
210	0.0538	0.076	0.881
240	0.0466	0.063	0.789
270	0.0378	0.049	0.690
300	0.0358	0.096	0.662

$$\text{Slope} = \frac{0.46}{160}$$

$$K_1 = \frac{2.303 \times 0.46 \times 1}{160 \times 60} \text{ sec}^{-1} = \underline{\underline{1.1 \times 10^{-4} \text{ sec}^{-1}}}$$

Table 3

1.33 gms. of Tolylazide and 1.40 gm. of Benzoyl Chloride made up to 50 mls. with Bromobenzene

Time	Weights	SCJ	Log of c
0	0.106	0.206	0.3139
15	-	-	-
60	0.140	0.192	0.283
90	-	-	-
120	0.0810	0.136	0.134
150	0.0714	0.112	0.0049
180	0.0617	0.090	0.959
210	0.0543	0.076	0.881
240	0.0421	0.055	0.740
270	0.0358	0.046	0.663
300	0.0309	0.039	0.591
330	0.0268	0.034	0.532
360	0.0224	0.027	0.431

$$\text{Slope} = \frac{0.26}{96}$$

$$K_1 = \frac{2.303 \times 0.26 \times 0.1}{96 \times 60} \text{ sec}^{-1}$$

$$= \underline{1.05 \times 10^{-4} \text{ sec}^{-1}}$$

Having established a nitrene mechanism the next objective was to check on the intermediacy of the N-chlorobenzanilides. A literature survey showed that N-chlorobenzanilide was synthesised by Orton and Chattaway [98] by treating benzanilide with sodium hypochlorite solution. We repeated this process several times and on each occasion obtained starting materials. However, a more recent method of Mitin and Vlasov [92] proved successful. This involved adding t-butyl hypochlorite to benzanilide suspended in methanol containing 10 ml of 4% borax solution. The mixture was thoroughly shaken and left in the dark for 2 hours after which time the N-chlorobenzanilide was obtained as a white solid (m.p. = 79°). The N-chlorobenzanilide was then thermolysed in benzoyl chloride under two different conditions. In the first case the benzoyl chloride employed was similar to that used in the thermolysis of the azides (i.e. free of hydrogen chloride) and in the second case it was saturated with dry hydrogen chloride. The reason for this dry hydrogen chloride was to attempt to make the medium similar to that of the decomposing azides, because, in most of these decompositions, hydrogen chloride was detected in the reaction mixture. In both cases quantitative yields of p-chlorobenzanilide were obtained. In fact this result only confirmed the early work of Orton, who showed that the N-chlorobenzanilide on heating to 120-130° yields only p-chlorobenzanilide together with benzoyl chloride.

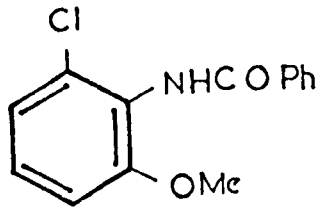
This result argues against direct insertion of the nitrene into the C-Cl bond, since on the basis of the above results, if the N-chloroanilide is formed then it should yield p-chlorobenzanilide, rather than the observed o-chloro isomer. The possibility of a radical or electrophilic chlorination giving rise to the o-chlorinated anilides was next considered.

p-Methoxyphenyl azide was employed in these experiments since it gives the highest yield of the o-chlorinated anilides, and should on the basis of electronic effects give an anilide with chlorine ortho to the methoxy group rather than or as well as ortho to the N-benzoyl function. Accordingly p-methoxyphenyl azide (7) was thermolysed in a mixture containing equal amounts of anisole and benzoyl chloride, and the products were separated by gas-liquid chromatography. No chlorinated anisoles were detected as shown by comparison of the gas-liquid chromatogram with a standard mixture of o-, m- and p-chloroanisole.

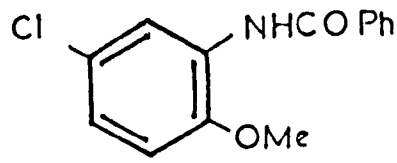
This result indicated that chlorination was not brought about by either radical chlorine nor was chlorination being caused by an electrophile, since if either were the case then chlorinated anisoles would be expected in the reaction mixture. Further, radical or electrophilic chlorine would not explain the ortho selectivity of chlorination particularly in the case of phenyl azide.

The apparent ortho selectivity of the halogenation process was clearly emphasised when o-methoxyphenyl azide was thermolysed in benzoyl chloride. Careful investigation of the tarry reaction residue produced only one product, a white solid (m.p. = 135°).

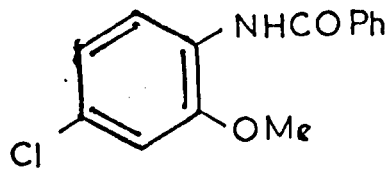
Mass spectral data showed it to have a molecular ion of 261 units with fragmentation losses of 35 and 105 units respectively. Infrared spectrum showed ν(NH) 3280 cm^{-1} and ν(CO) 1655 cm^{-1} features indicative of an amide. From the information the product could be any one of the four possible chloroanilides shown overleaf of which on the basis of electronic and steric effects, and assuming an electrophilic process, the 2-methoxy-5-chloro-isomer (34) would possibly be the most favoured.



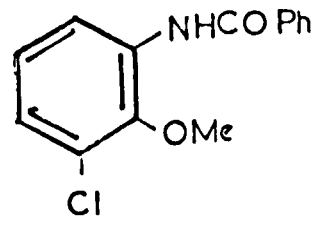
(33)



(34)



(35)

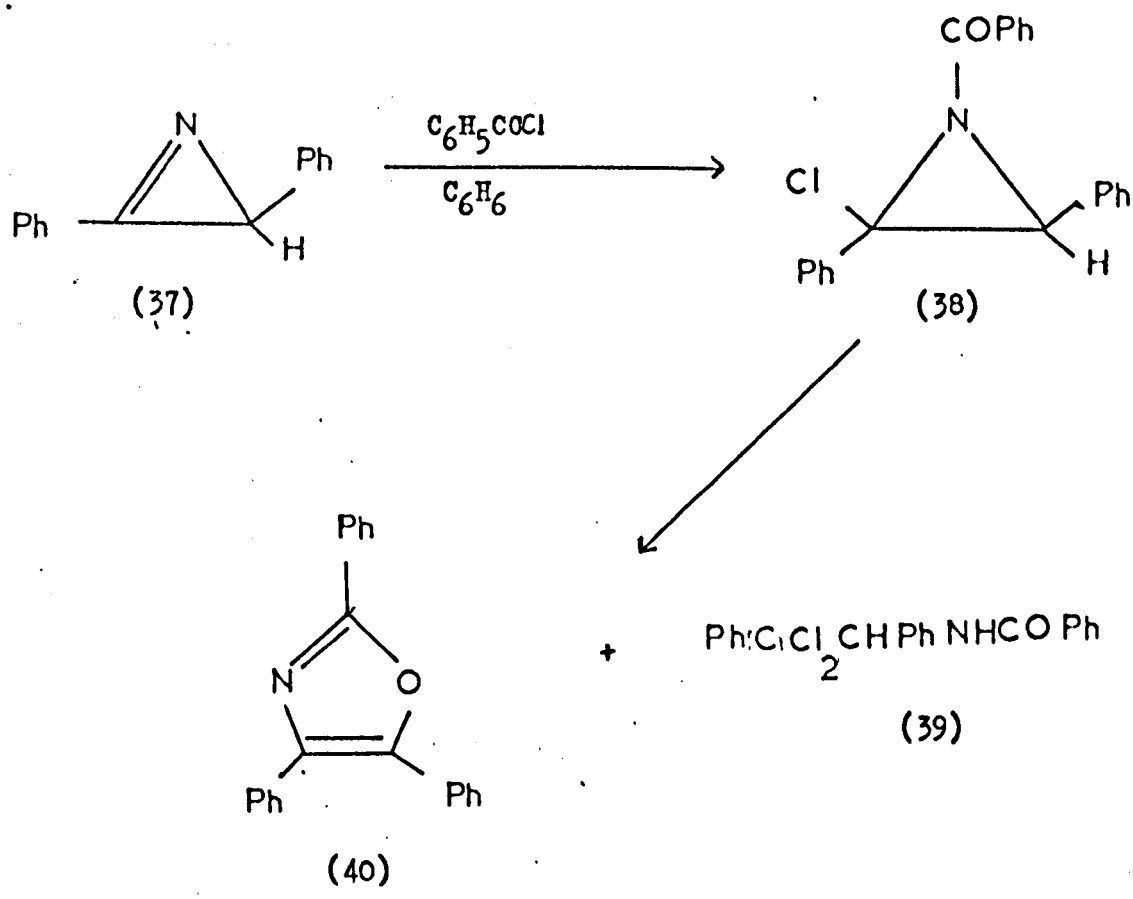


(36)

Synthesis of N-benzoyl-3-chloro-6-methoxyaniline (34) (m.p. = 77°) was achieved by benzoylation of commercially available 4-chloro-2-aminoanisole and its infrared spectrum was non-superimposable with that of the reaction product. However, N-benzoyl-2-chloro-6-methoxyaniline (33), synthesised by the benzoylation of 2-amino-3-chloroanisole, on the basis of its infrared spectrum and a mixed melting point (m.p. = 134°) was shown to be identical to the azide decomposition product. This result has shown quite conclusively that chlorination does not take place by a radical or an electrophilic process, and we now propose some possible mechanisms by which the ortho-chlorinated anilides may arise.

There is reasonable evidence [47] that the singlet nitrene initially formed by the thermal decomposition of aryl azides is in equilibrium with the azirine (41). This azirine can react with benzoyl chloride to give the unstable adduct (42). An analogous reaction has been investigated by Fowler [102] who showed that 1-azirines (e.g. 37) will react with carboxylic acid chlorides to give N-benzoyl-2-chloroaziridines (e.g. 38) which under the reaction conditions are unstable and are converted into a mixture of dichloroamide (39) and the oxazole (40) as shown in Scheme 7.

SCHEME 7

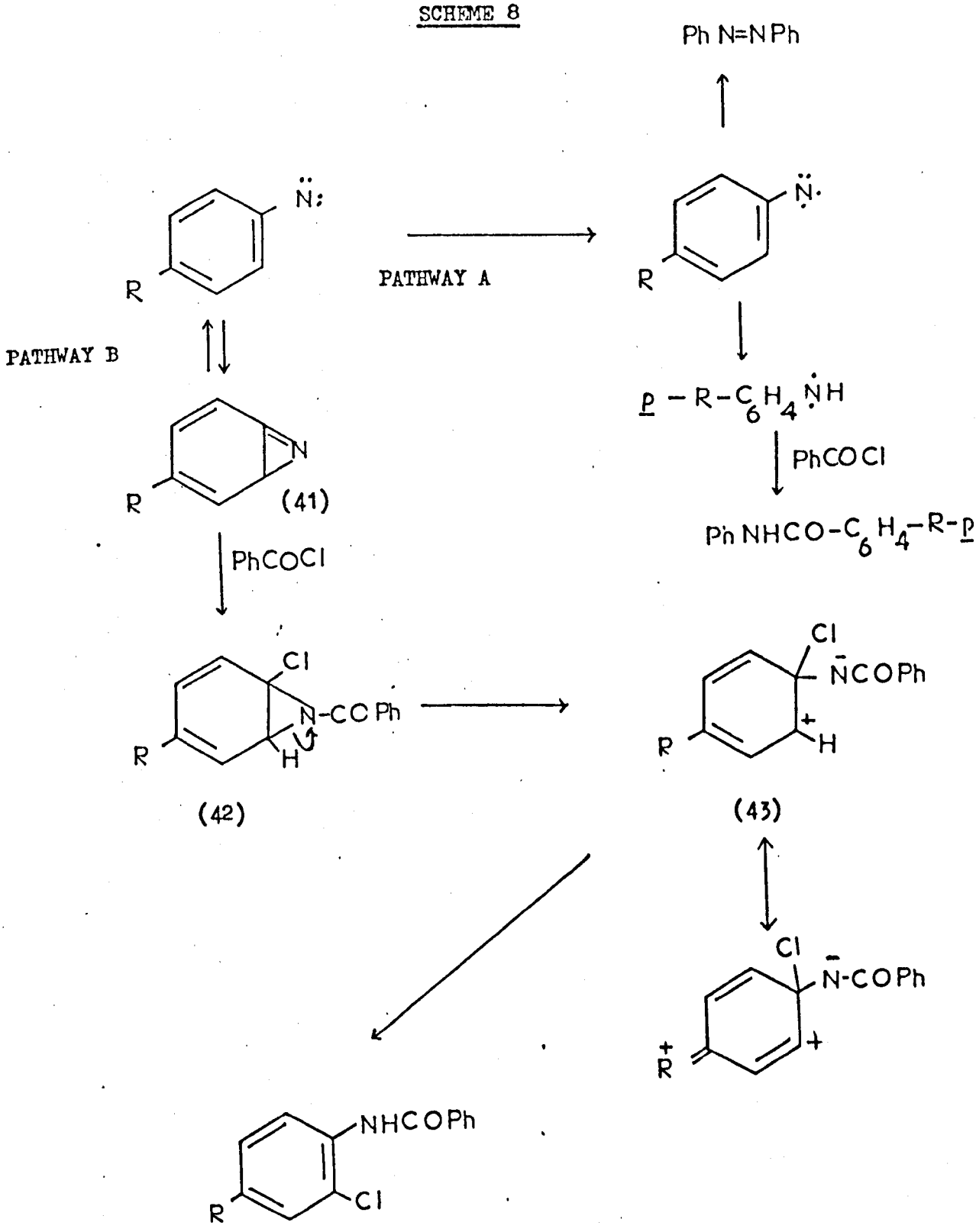


(37) (38) (39) (40)

For example, where the substituent R is electron donating, (e.g. MeO) the chloro-aziridine intermediate can open not by an electrocyclic process as in the case of azepine formation [3] but by heterolysis of the carbon-nitrogen bond to give the resonance stabilized dipolar Zwitterionic species (43). This can then undergo a 1,2-chloride shift and proton transfer to yield the o-chlorobenzanilides as shown in Scheme 8.

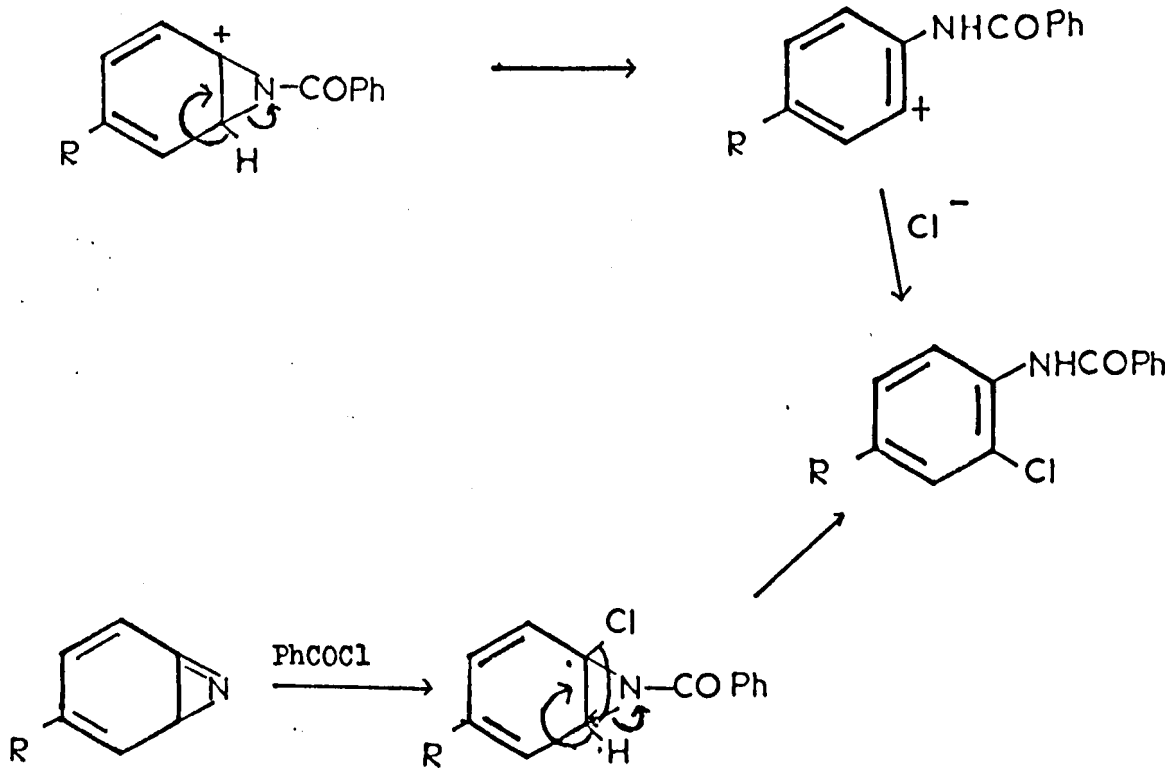
Similar results have been invoked by Abramovitch and his co-workers [103] to explain the intermolecular substitution reactions of aryl- and sulphonyl nitrenes with aromatic substrates.

SCHEME 8


Ph N=NPh
PATHWAY A
PATHWAY B
R
(41)
PhCOCl
p – R – C6H4 NH
PhNHCO – C6H4 – R – p
Cl
N-CO Ph
H
(42)
NCOPh
(43)
NHCOPh

Alternatively attack of the chloride ion may take place after ring opening or it may be concerted with the opening of the aziridine ring, as in Scheme 9.

SCHEME 9



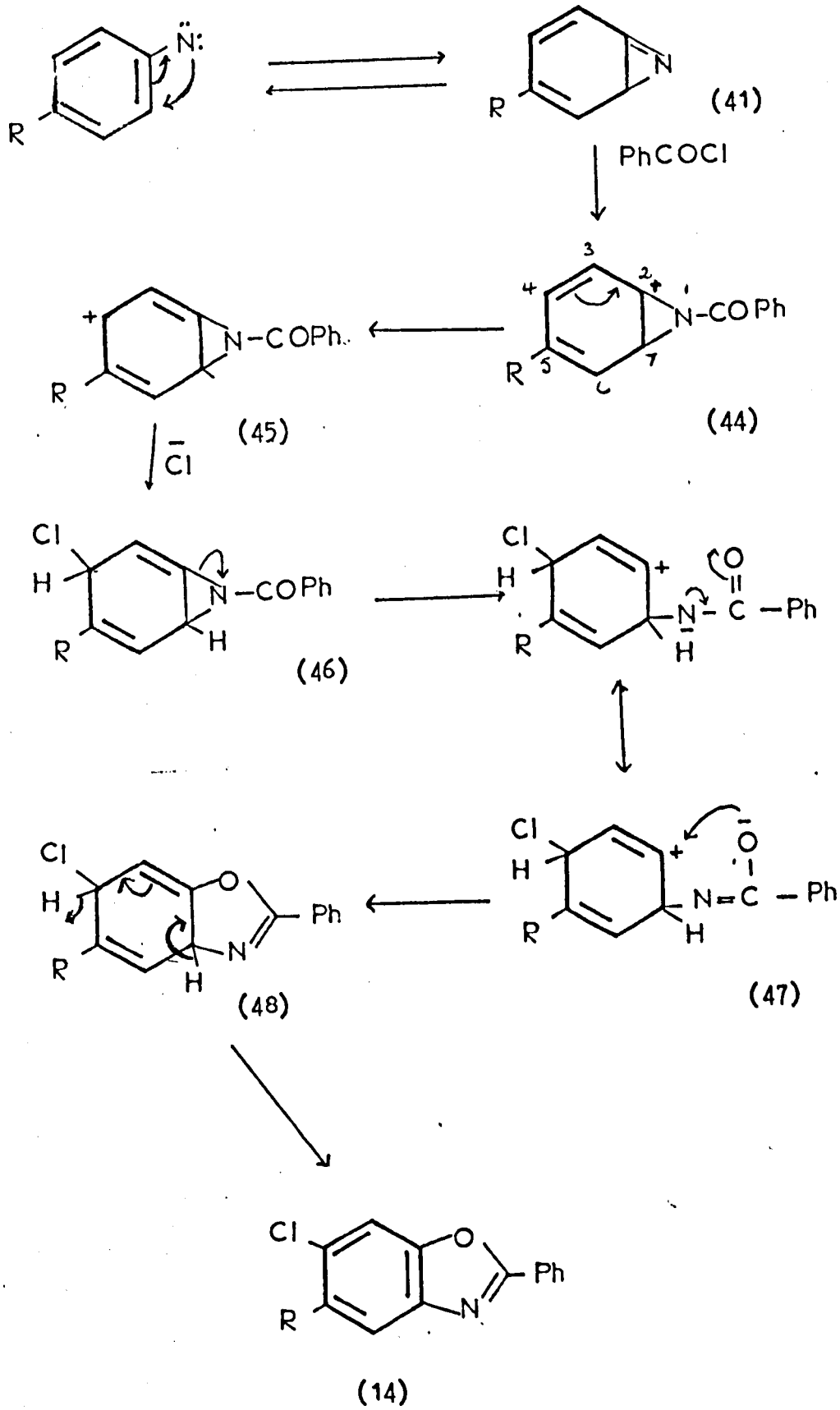
Scheme 8 can explain the decrease in yield of the o-chloroanilide as the electron donating nature of the para substituent (R) (i.e. its ability to stabilize the positive charge) decreases (i.e. in the order MeO > Me > H > Cl). Azirine formation is a consequence of singlet nitrene formation and hence if the chloro-compound derives via an azirine i.e. a singlet nitrene, then the yield of the chloroanilide should increase or be unaffected on carrying out the decomposition of the aryl azide in the presence of a triplet quencher. By the

same reasoning the yields of aryl triplet base products should decrease. It was decided, therefore, to decompose phenyl azide in benzoyl chloride in the presence of a triplet quencher. The most suitable for this system was molecular oxygen [104] since it had no action on the acyl chloride. Accordingly phenyl azide was made to decompose in boiling benzoyl chloride under oxygen. 2-Chlorobenzanilide was obtained in undiminished yield whereas the triplet based products were isolated in drastically reduced amounts. Benzanilide was obtained in 20% compared with 50% whereas azobenzene (originally isolated in 2%) could not be detected in the reaction mixture. The only remaining product not accounted for was 6-chloro-2-phenylbenzoxazole (14). It is interesting to note that this type of product is only obtained from the decomposition of phenyl azide. It was first thought that this benzoxazole originated by the interaction of the nitrene with benzoic acid generated in the reaction mixture. Such a reaction would be similar to the oxazole formation investigated by Suschitzky and his co-workers [90] who obtained benzoxazoles by decomposing aryl azides in a mixture of benzoic acid and polyphosphoric acid. However, introduction of benzoic acid into the reaction mixture failed to improve the yield of the chlorobenzoxazole (14) and in fact only intractable tars were obtained from this decomposition. A literature survey revealed that electrophilic substitution [105] of 2-substituted benzoxazoles occurs mainly at the 5- and 6- positions, although no examples of direct chlorination appear to have been reported. The known chlorobenzoxazoles appear to have been prepared from chlorine containing precursors. However, nitration of 2-methylbenzoxazole [106,107] gives a mixture of the 6-, and 5-nitro isomers showing clearly that it is the 5, and 6- positions which are

open to electrophilic attack. On this basis we considered the chlorophenylbenzoxazole to arise by electrophilic attack on a preformed benzoxazole nucleus. However, this idea was precluded on the basis of the decompositions in the presence of anisole discussed earlier.

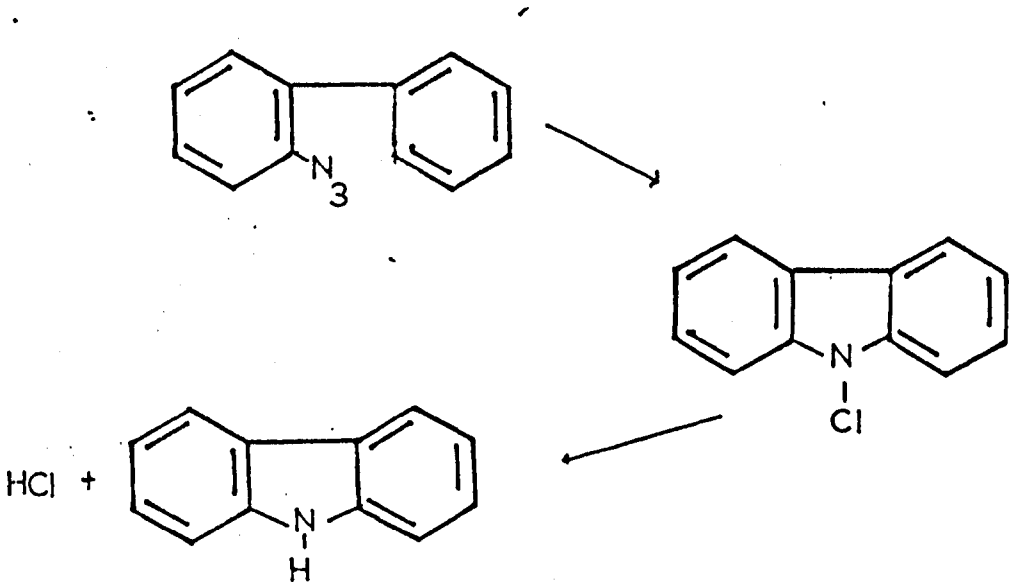
A tentative scheme to explain the formation of the 6-chloro-2-phenylbenzoxazole is as follows: As in the formation of the o-chlorinated benzanilides an azirine (41) is postulated, which can react with benzoyl chloride to give the adduct (44). When R=H, the stabilization of the positive charge in the 7-position is less favourable than where R is electron donating. Instead an alternative mesomer may be drawn in which the electron deficiency lies at the 4-position (see diagram 45). Attack by nucleophilic chlorine (Cl) at this position gives rise to the intermediate (46) which, on heterolytic ring opening of the aziridine and recyclisation in the manner indicated (46 - 48), yields the dihydrooxazole (48). Aromatisation via a 1,4-hydrogen loss then yields the product, 6-chloro-2-phenylbenzoxazole (14). This ring opening of the N-acyl aziridines to give oxazoles is a well documented process.[107,108] These reactions are summarised in Scheme 10.

SCHEME 10



The formation of carbazole and N-benzoylcarbazole from the decomposition of 2-azidobiphenyl is as predicted on the basis of the known behaviour of o-azidobiphenyl. The nitrene once formed intramolecularly abstracts hydrogen from the 2-position of the other phenyl ring with subsequent ring closure, a feature well documented [79] in the decomposition of this azide in other solvents. A possible alternative method of forming carbazole in which the N-chloroanilide is formed, followed by cyclisation with loss of hydrogen chloride is unlikely in view of previous discussions.

SCHEME 11

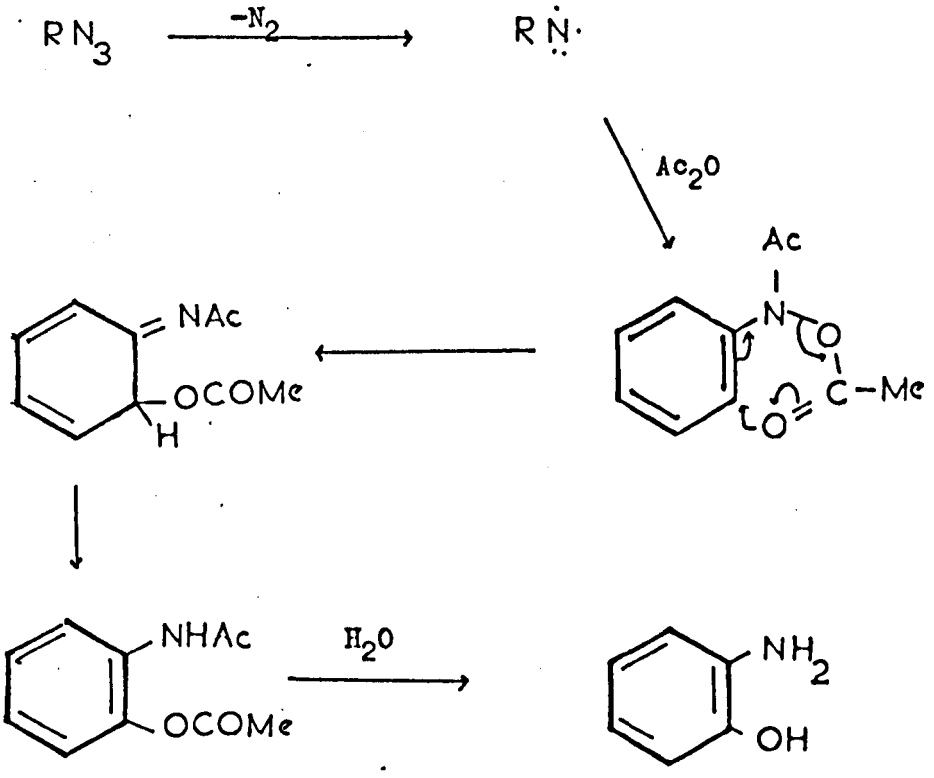


Also a blank experiment showed that carbazole in boiling benzoyl chloride yields the N-benzoyl derivative. These findings were substantiated when the azide (12) was thermolysed in boiling acetic anhydride. Once again carbazole was formed almost quantitatively, along with a small amount of N-acetylcarbazole.

The consideration that the azirine intermediates are concerned in the formation of o-chlorobenzanilides has thrown new light on the formation of o-aminophenols in the decomposition of aryl azides in acetic anhydride.

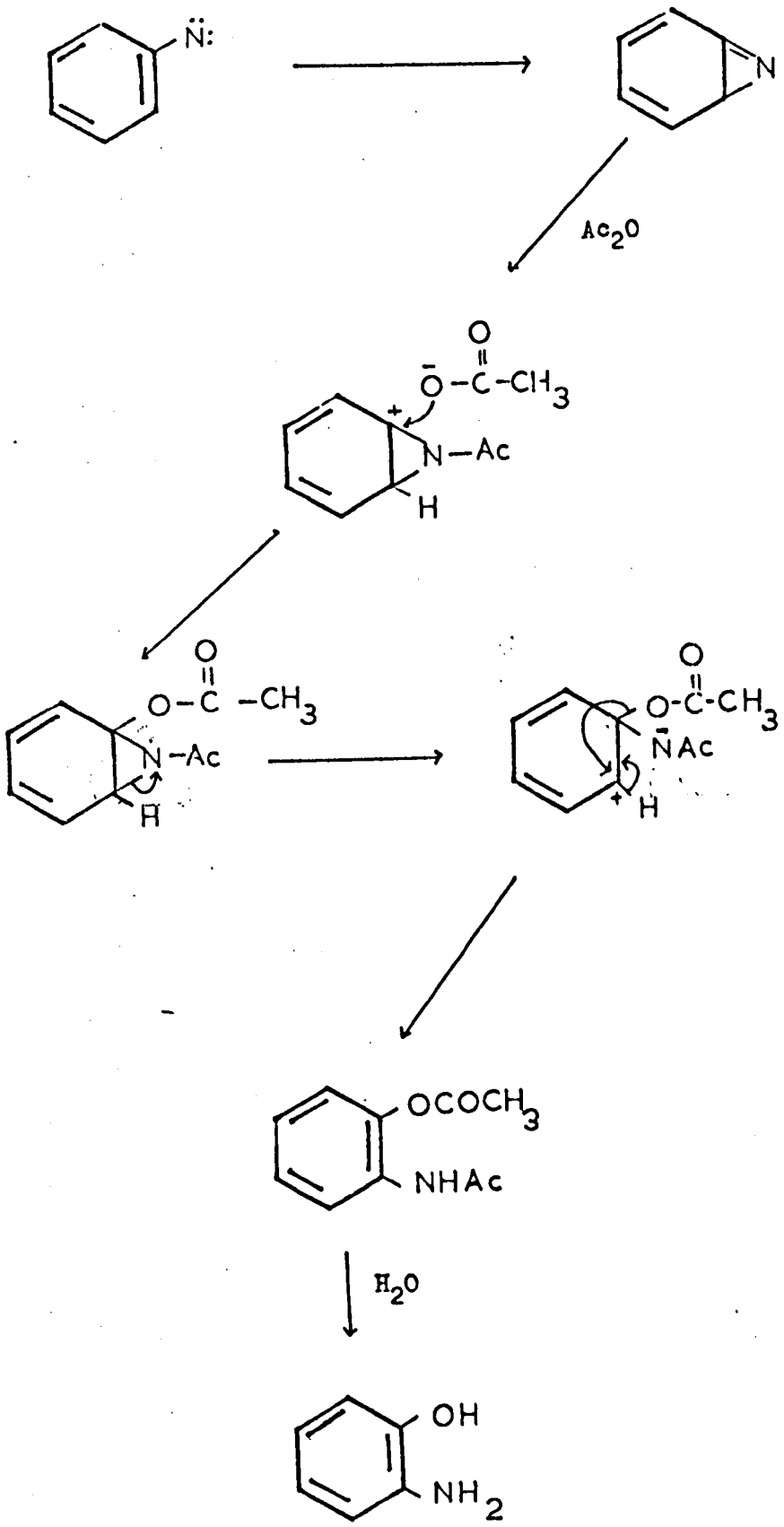
Smalley and Suschitzky [83] suggested that the o-aminophenols are formed via the N, O diacylhydroxylamines as shown in Scheme 12.

SCHEME 12



While there is no doubt that the N,O-diacylhydroxylamines rearrange on heating to give o-aminophenols [109], a route similar to that put forward to explain the formation of o-chlorobenzanilide is now favoured to explain o-aminophenol formation, as outlined in Scheme 12. In support of this mechanism is the recent work of Fowler [102] who demonstrated that addition of acetic anhydride and benzoyl chloride to 1H-azirines to give N-acetyl and N-benzoyl aziridines is facile. Further Sundberg and Smith [110] have recently shown that nitrosobenzene and o-, and p-nitrotoluene on thermolysis in a mixture of acetic anhydride and triethyl phosphite yield the respective o-acetoxyacetanilides. They showed that the O, N-diacetylhydroxylamines were not the intermediates in these reactions and that the products from these thermolyses arose from nucleophilic aromatic substitution processes.

SCHEME 13


N:
N
Ac2O
O
O-C-CH3
N-Ac
H
O
O-C-CH3
N-Ac
H
O
O-C-CH3
NAc
H
OCOCH3
NHAc
H2O
OH
NH2

Photolysis of Aryl Azides in Benzoyl Chloride

The photolysis of aryl azides in amine solution to give azepines is well documented [7,10] but no work has been reported on the photolytic decomposition of aryl azides in an acid chloride solution. Having shown that aryl azides thermally decompose in benzoyl chloride to give mainly o-chlorobenzanilides, we decided to investigate their photolysis in the same medium in order to compare and contrast the modes of decomposition.

Phenyl; p-methylphenyl-, p-methoxyphenyl-, and p-chlorophenyl azide as 1% solutions in benzoyl chloride were photolysed for forty-eight hours using a 125 Watt mercury lamp fitted with a pyrex filter. In each case the azide was recovered unchanged. However, when a quartz filter was employed in these photolytic decompositions and the solutions irradiated for twenty-four hours the azides decomposed to give predominantly polymeric materials. In fact only in the case of p-methoxyphenyl azide were products isolated. viz. 4,4'-dimethoxy-azobenzene and N-benzoyl-2-chloro-4-methoxyaniline, i.e. the same products as from the thermolyses reaction but in greatly reduced yields.

Possibly the poor results are due to the fact that the majority of the light energy is being absorbed by the acid chloride. In fact Swenton [111] has shown that when aromatic azides are irradiated, the energy is first absorbed into the aromatic system and then transferred to the azido group. In the cases where pyrex filters were employed, the energy may be preferentially absorbed by the acid chloride and consequently no energy reaches the azides. However, the use of a quartz filter allows through radiation of increased wavelength, which, although giving some products in one case, is so intense as to lead mainly to polymeric formation.

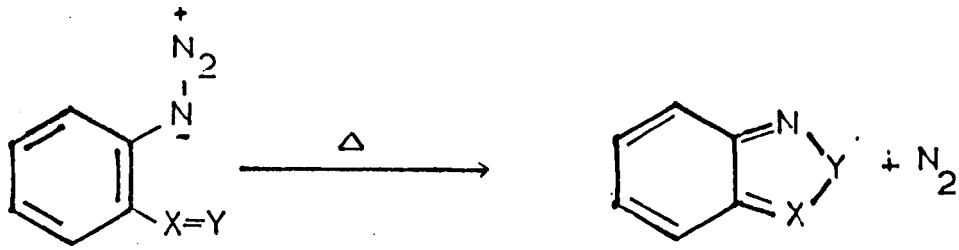
Thermolysis of Benzoyl Azide in Benzoyl Chloride

In the light of recent work by Smalley and Bingham [112] who showed that the decomposition of benzoyl azide in hot acetic anhydride gave N,N-diacetylaniline in quantitative yield, it was of interest to investigate the decomposition of benzoyl azide in boiling benzoyl chloride. Like the previous authors it was found that the azide undergoes Curtius rearrangement to give the phenyl isocyanate, but whereas in acetic anhydride further reaction is observed, in benzoyl chloride the reaction ceases and the isocyanate is the sole product.

CHAPTER 3

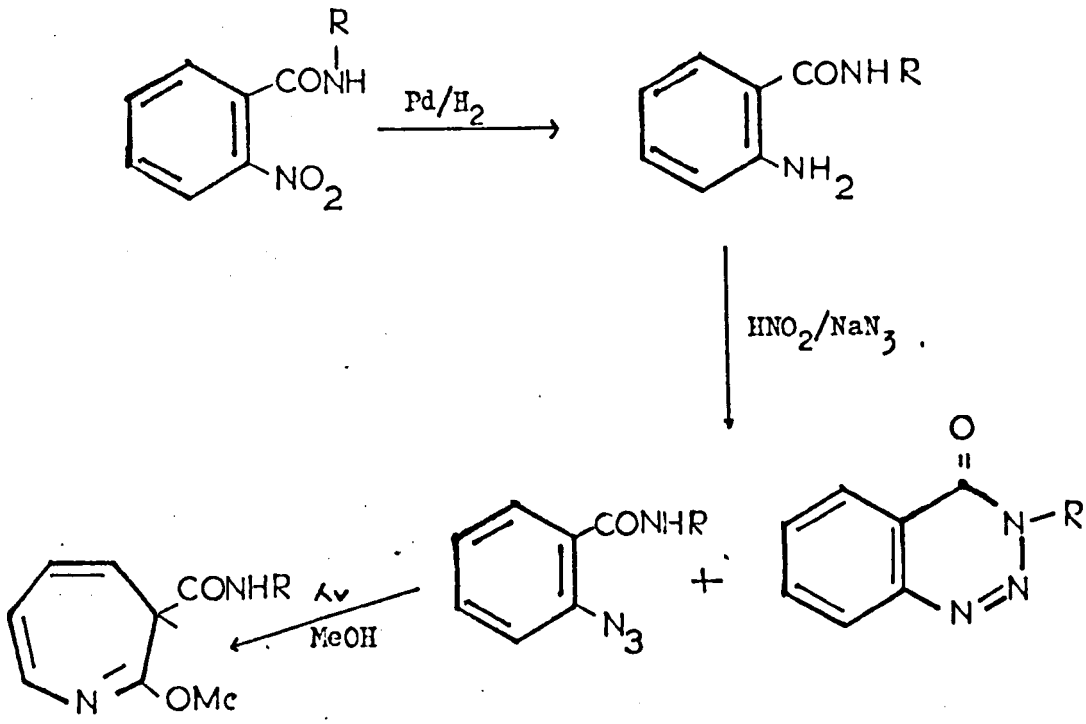
Synthesis and Decomposition of Ortho-Azido Carbonyl Compounds

Many aromatic azides with an unsaturated ortho-substituent can be pyrolysed to yield cyclic products as shown in the general scheme below



Examples where the ortho substituent is nitro, [40,113,117] phenylazo [114,115] phenyl, [12,116] thiophenyl, [12] phenylsulphonyl [12] azomethine [117,118] and carbonyl [119,120] have led to benzotriazoles, carbazoles, phenothiazines, phenothiazine dioxide, benzimidazoles or indazoles and anthranils, respectively. Most of these decompositions are well documented but it is interesting to note that anthranils are obtained from o-azidoketones (o-N_3-Ph-CO-R where R = CH_3 and Ph). Recently it has been shown that o-azido acetophenone [15] will undergo photolytic decomposition in methanol to give 3-acetyl-2-methoxy-3H-azepine in 58% yield, and in piperidine to give a mixture of 3-acetyl-2-piperidino-3H-azepine and the isomeric 7-acetyl-2-piperidino-3H-azepine. Similarly, o-azido amides [6] on photolysis in methanol give 2-methoxy-3H-azepine-3-carboxamides as shown in Scheme 1.

SCHEME 1

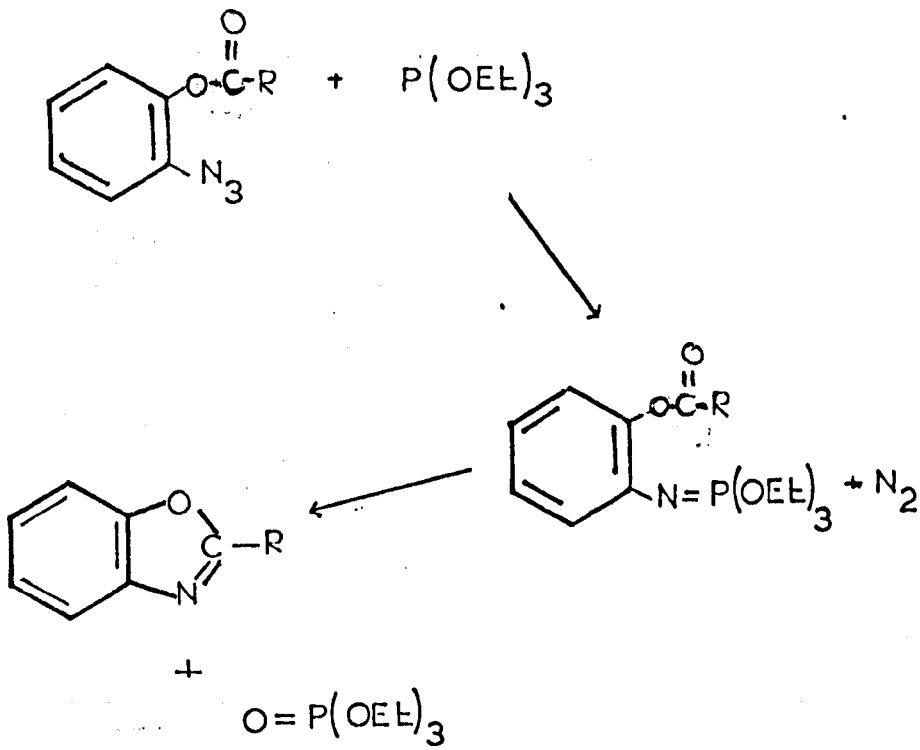


(R values on p. 14, Chapter 1.)

A literature survey revealed that with the exception of the above results and some early work on o-azidobenzoic acid and the esters, mentioned below, little information concerning the decomposition of o-azido-carbonyl compounds e.g. esters, anhydrides, etc. is available. o-Azidobenzoic acid has been synthesised by various workers [121,122] although its thermal decomposition does not appear to have been investigated. In fact the most interesting property of this acid comes from the work done by Smith and his co-workers [122] who showed that the azido group is acid-strengthening due to its electron withdrawing effect. o-Azido esters [123] on thermal decomposition have been reported to give tars. However, reductive cyclisation [124] of o-azidophenyl benzoate (1) and

o-azidophenyl acetate (2) in a mixture of triethyl phosphite and cyclohexane have led to the formation of 2-phenylbenzoxazole and 2-methylbenzoxazole in yields of 71% and 69% respectively. (Scheme 2; R = Ph and Me).

SCHEME 2



It appears, therefore, that no systematic investigation of the decomposition of o-azido-carbonyl compounds has been carried out. Accordingly we decided to investigate the thermolytic and photolytic decompositions of selective examples of o-azido-carbonyl compounds and then to discuss the results in a systematic manner.

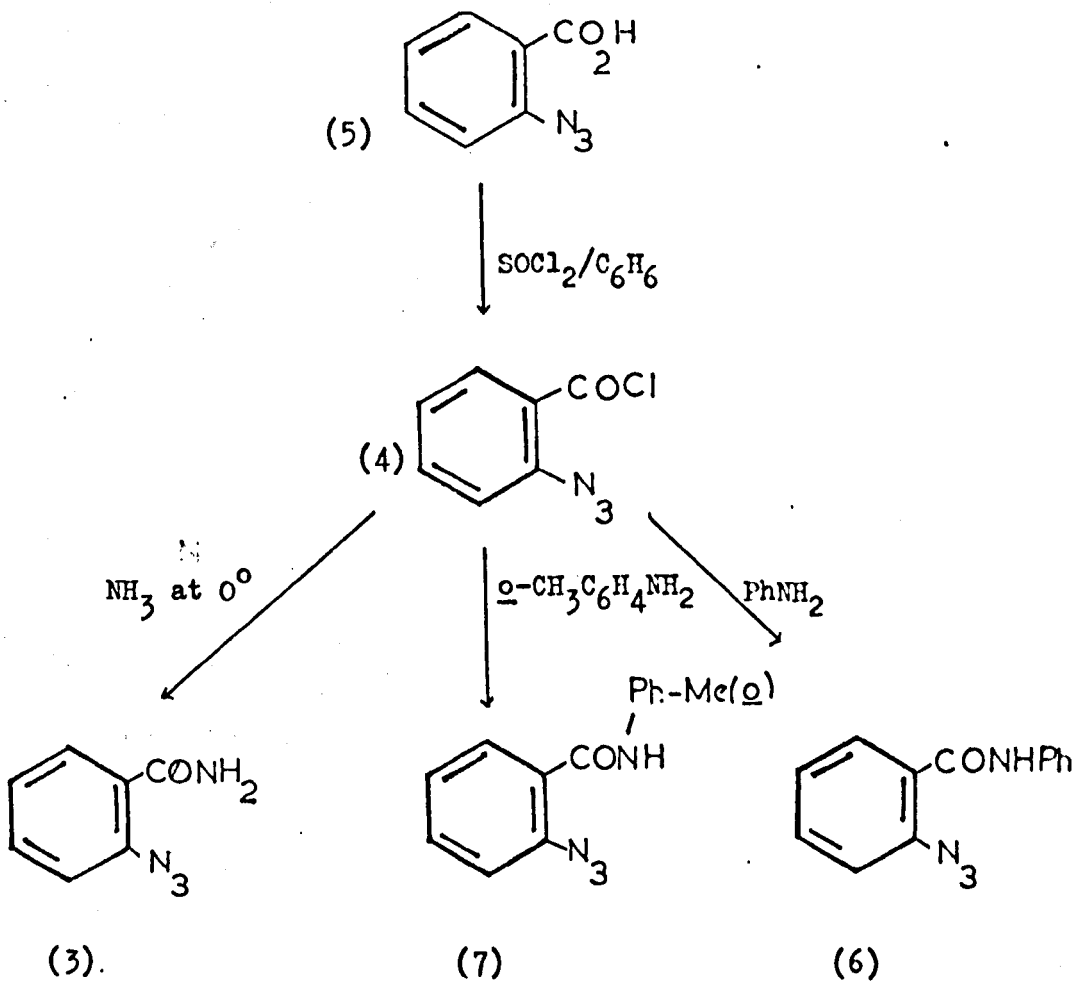
a) Synthesis of o-Azido-Amides

The first reported synthesis of an o-azido-amide was achieved by Bamberger and Demuth.[125] These workers obtained 2-azidobenzamide (3) by a Beckman rearrangement of 2-azido benzaldoxime. More recently this azide and other related compounds [16] have been synthesised from the respective o-nitro-benzamides as shown in Scheme 1. This method has the disadvantage that diazotisation of the o-aminobenzamides not only led to poor yields of the o-azidobenzamides, but in some cases intramolecular cyclisations to give 3-alkyl-1,2,3, benzotriazin-4 (3H)- ones are also observed. In fact when (R = Ph) (Scheme 1) the benzotriazinone (R = Ph) is the sole product. A possible alternative method for the synthesis of o-azido-amides is the reaction of o-azidobenzoyl chloride (4) with an amine in a suitable solvent (e.g. sodium hydroxide). The hitherto unreported 2-azidobenzoyl chloride (4) was synthesised by treating o-azidobenzoic acid (5) with freshly distilled thionyl chloride in dry benzene. The azido acid chloride was isolated as a pale yellow oil, which proved difficult to purify in that it was susceptible to hydrolysis, and attempted distillation at 70° and 0.05 mm pressure failed. In view of the hazards associated with the distillation of o-nitrobenzoyl chloride [126] further distillation attempts were not pursued. This azide was characterised by the infrared spectrum, ν(C=O) at 1790 and 1750 cm^{-1} and $\nu(N_3)$ at 2150 cm^{-1}, and mass spectral data (i.e. Mol Ion).

It was also characterised by its conversion to the known 2-azidobenzamide (3) by reaction with cold concentrated ammonia solution, and the formation of N-(o-azidobenzoyl) aniline (6) and N-(o-azidobenzoyl)-o-toluidine (7) from aniline and o-toluidine

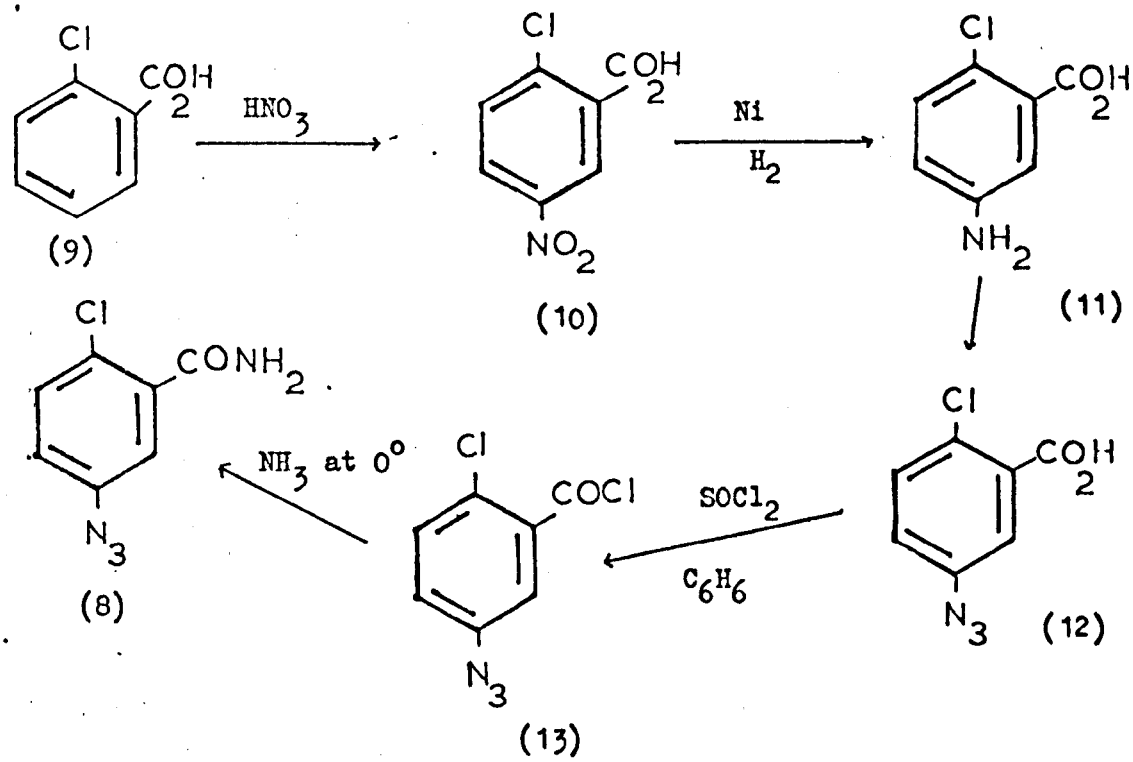
respectively in sodium hydroxide solution. These reactions are summarised in Scheme 3.

SCHEME 3



A fourth amide 5-azido-2-chlorobenzamide (8) was also synthesised (the purpose of which will be discussed later). Nitration of 2-chlorobenzoic acid, afforded 2-chloro-5-nitrobenzoic acid (10). The acid was reduced with Raney Nickel and hydrogen to give 5-amino-2-chlorobenzoic acid (11) which was converted to 5-azido-2-chlorobenzoic acid (12) via the diazonium compound. Treatment of this acid with thionyl chloride followed by ammonia solution led to 5-azido-2-chlorobenzamide (8). These reactions are summarised in Scheme 4.

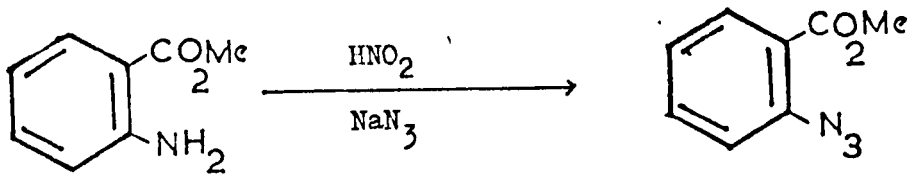
SCHEME 4



b) Synthesis of ω-Azido-esters and Thioesters

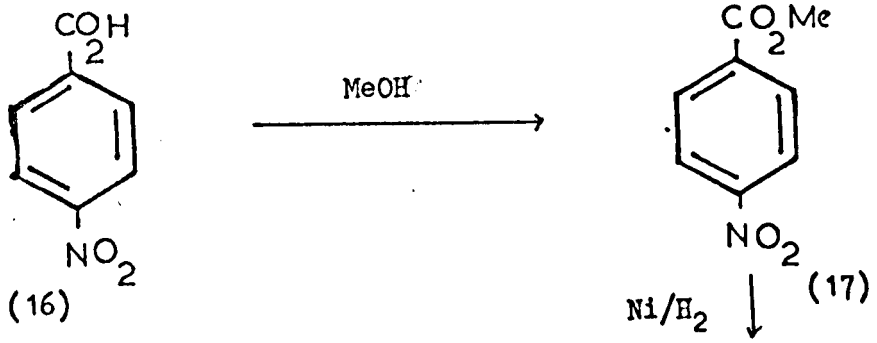
Two standard methods were employed in the preparation of these esters. The first and most common was the diazotisation of the amino-esters followed by treatment with sodium azide. In all cases except one (i.e. Methyl anthranilate) the amino-esters had first to be synthesised. Their synthesis was easily accomplished by reduction of the corresponding nitro compound as outlined in the following Schemes (5a-c).

SCHEME 5a



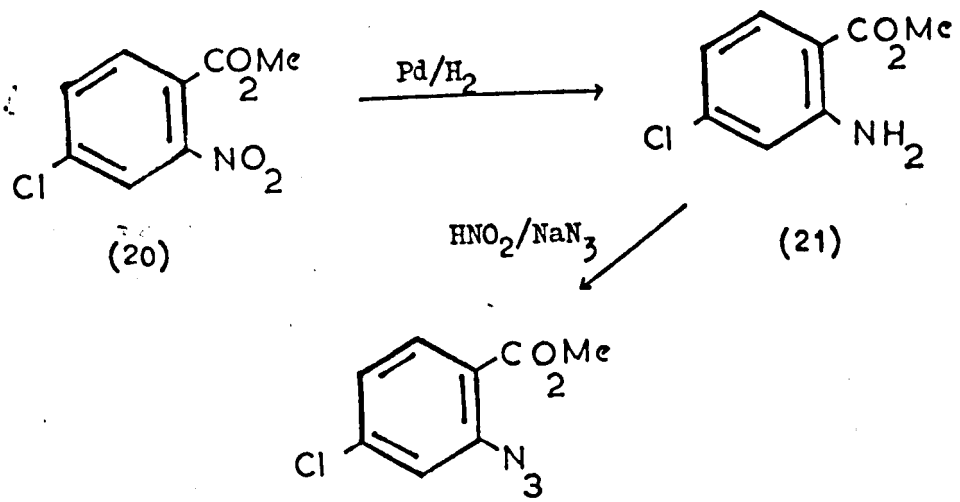
(14) (15)

SCHEME 5b



(16) (17) (18) (19)

SCHEME 5c

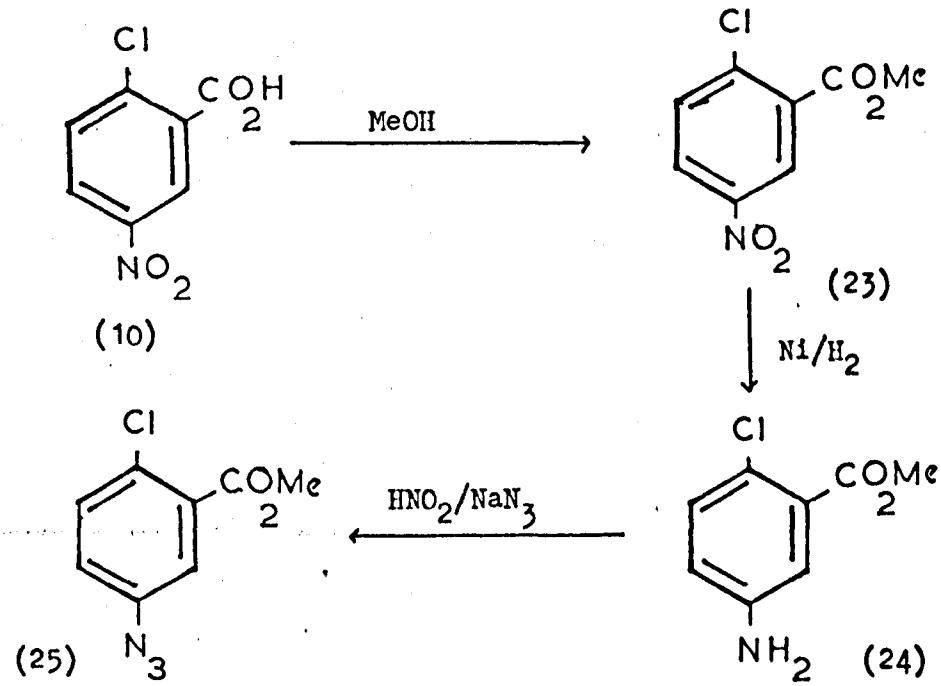


(20) (21) (22)

The azido-esters (15) and (19) were identical to those synthesised by Majewski and Rupe.[127] However, the chloroazido-ester had not been reported previously, and was characterised by spectroscopic (mass and infrared) and analytical data.

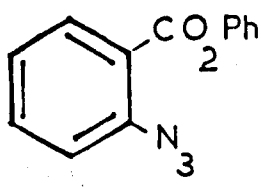
Also prepared was Methyl 5-azido-2-chlorobenzoate (25) and its synthesis is outlined in (Scheme 6).

SCHEME 6

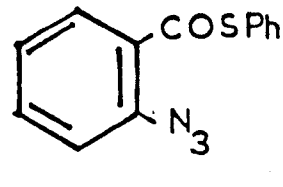


This azide (25) was again characterised by means of mass and infrared spectral data and by elemental analysis.

Phenyl o-azidobenzoate (26) and the corresponding thiophenyl ester (27) were prepared by treating 2-azidobenzoyl chloride with phenol and thiophenol respectively under Schotten-Baumann conditions.



(26)



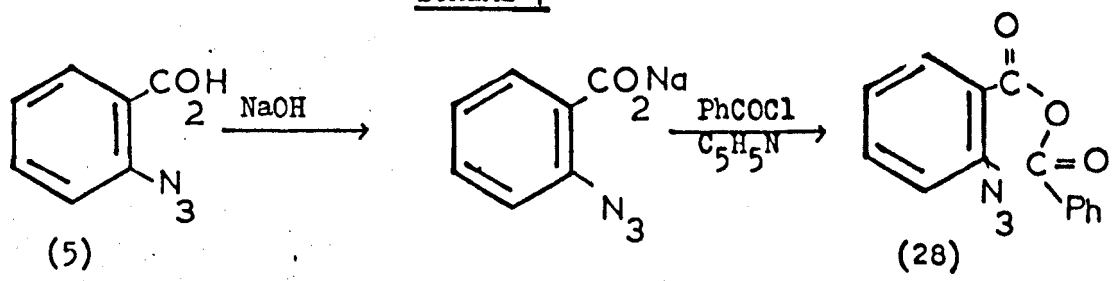
(27)

The decomposition of azide (26) has been reported by Dyall and Kemp [124] but no synthetic nor analytical data for the azide were given. This compound was obtained as a white solid m.p = 50° and its structure was confirmed by infrared and mass spectral evidence along with elemental analysis. The structure of the hitherto unreported azido-thioester (27) (m.p. = 78°) was also borne out by analytical data i.e. molecular formula $C_{13}H_9N_3OS$, and a molecular ion 255^+ from the mass spectra. The strong absorption at 2240 cm^{-1} in the infrared spectrum confirms the presence of the azido group whereas the carbonyl group appears as a low intensity band at longer wavelength (1685 cm^{-1}). This low intensity and the position of the carbonyl group in thioesters has been explained by Nakanishi.[128] This is due to the +M effect of the sulphur which is larger than its -I effect and accounts for the decreased frequencies as compared to standard values of saturated aliphatic ketones (i.e. 1715 cm^{-1}).

c) Synthesis of o-Azidobenzoic acids, o-Azidobenzoic Anhydride and o-Azidobenzophenone

o-Azidobenzoic anhydride (28) was prepared by the Smalley and Suschitzky method [129] as outlined in Scheme 7. This method is applicable to anhydrides which are unaffected by cold water and involves shaking an aqueous solution of the alkali-metal carboxylate with an acyl halide at room temperature in the presence of a few drops of pyridine.

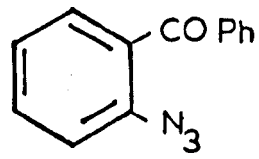
SCHEME 7



(5) (28)

This azide was obtained as a yellow liquid and its structure was confirmed by infrared evidence ν(CO) at 1820 and 1750 cm^{-1} and ν(N_3) at 2145 cm^{-1}; mass ion of 267 from mass spectrometry and the molecular formula $C_{14}H_9N_3O_5$ from analytical data. On standing the anhydride slowly hydrolyses to give 2-azidobenzoic acid and benzoic acid.

2-Azidobenzoic acid (5) and 5-azido-2-chlorobenzoic acid (12) were prepared from the respective amines as indicated previously. 2-Azidobenzophenone (29) was prepared by the method outlined by Smith and his co-workers [12] i.e. by diazotisation of 2-aminobenzophenone and treatment of the diazonium solution with sodium azide.



(29)

d) Thermolysis of o-Azido-carbonyl Compounds

The o-azido-carbonyl compounds were thermolysed in various solvents and the products obtained from the decompositions are shown in Table 1.

Table 1

Products of Thermolysis of o-Azido-carbonyl Compounds

R	Solvent	Products	Yield %
OMe	bromobenzene	a) 2,2'-bis(methoxycarbonyl)azobenzene b) methyl anthranilate	4 6
OPh	bromobenzene	2,2'-bis(phenoxycarbonyl)azobenzane	1%
OH	bromobenzene	Polymeric materials	-
Ph	chlorobenzene	3-phenylanthranil	91
NH_2	bromobenzene	Polymeric materials	-
NHPh	"	"	-
SPh	"	diphenyl disulphide	20

As found by Dyall and Kemp, [124] the o-azido-esters gave predominantly polymeric materials. In fact the only isolable products from the decomposition of methyl o-azidobenzoate and phenyl o-azidobenzoate in bromobenzene were the corresponding azo compounds and amines. As expected o-azidobenzophenone decomposed to give 3-phenyl-anthranil (30) in high yield but o-azidobenzoic acid, o-azido-benzamide, and o-azidobenzanilide gave only polymeric materials. Finally the 2-azidophenylthioester (27) on thermolysis in bromobenzene gave diphenyl disulphide (31) as the sole non-tarry product.

e) Photolysis of o-Azido-carbonyl Compounds in Alcohols

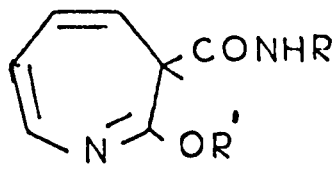
Stevens and Mair,[16] as previously indicated in Chapter 1, obtained 3H-azepines from the photolysis of selected o-substituted benzamides in methanol and one of the azides they were unable to synthesise was N-(2-azidobenzoyl)aniline. It was, therefore, fitting that this was the first azide to be photolysed, and yielded the anilide of 2-methoxy-3H-azepine-3-benzoic acid (32) (see Table 2) together with a trace of methyl anthranilate. The structure of this 3H-azepine followed from the following evidence. The appropriate molecular ion 242^+ was obtained in the mass spectrum. The infrared spectrum then showed the presence of the amidic function ν(NH) at 3290 cm^{-1} and ν(CO) at 1670 cm^{-1} together with absorption at 1615 cm^{-1} due to the (C=N) function. Analytical data showed the compound to have the molecular formula $C_{14}H_{14}N_2O_2$.

The informative evidence for the azepine structure comes from the ^1H. nuclear magnetic resonance spectrum. The singlet at τ6.25 is attributable to OMe and the doublet at τ.6.54 is assigned to the 3-proton ($J_{3,4}$ 6.5H_z). The olefinic protons appear at τ 3.3-4.2 and a low field doublet τ 2.9-3.1 is attributable to H-7 ($J_{6,7}$ 7.9H_z). Finally absorption at τ 2.2-2.8 was a multiplet due to aromatic protons. This result is in accord with the work done by Stevens and Mair.[16] 3H-Azepines are well documented as discussed in Chapter 1. The full mechanistic implications of these results are discussed later in this section. However, the reaction appears to involve addition of methanol across the azirine intermediate followed by ring expansion. On this basis there appeared to be no reason why other alcohols could not be used as a solvent and

hence lead to a convenient synthesis of 2-alkoxy substituted azepines. Accordingly, several o-azido-amides have been photolysed in a variety of alcohols and the yields of the resulting 2-alkoxyl-3H-azepine-3-carboxyanilides are given in Table 2.

Table 2

2-Alkoxy-3H-azepines-3-carboxamide



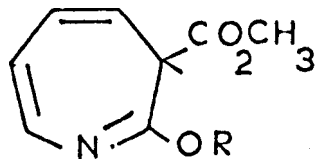
R	R'	m.p.	Yield %
Ph	Me	159	60
Ph	Et	111	40
o-Me C_6H_4	Et	150	55
H	Et	153	81
H	propyl	122	67

32. R = Ph, R^1 = Me
33. R = Ph, R^1 = Et
34. R = o-Me C_6H_4, R^1 = Et
35. R = H, R^1 Et
36. R = H, R^1 = propyl

The o-azidotoluide (7) was of potential interest in that insertion of the nitrine into the methyl group could compete with azepine formation. However, no insertion products were observed as can be seen from Table 2, and a 55% yield of the azepine resulted. In view of these results we decided to photolyse the o-azido-esters in various alcohols and found that they behaved in a like manner to the o-azido-amides, and gave 3-alkoxycarbonyl-2-alkoxy-3H-azepines in good yields as can be seen from Table 3.

Table 3

3-Alkoxycarbonyl-2-alkoxy-3H-azepines



R	b.p (mm)	Yield %
CH_3	75/0.5	58
Et	120/0.4	67
propyl	130/1	66
isopropyl	100/3	59
butyl	110/0.1	72

37. R = CH_3

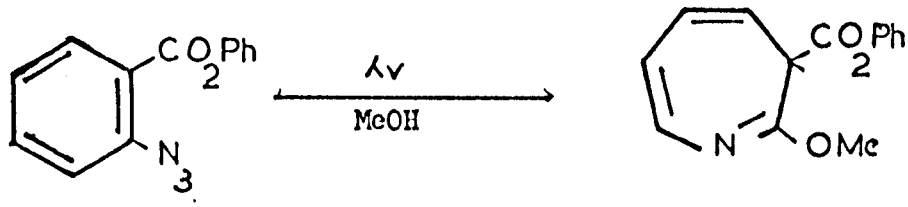
38. R = Et

39. R = propyl

40. R = isopropyl

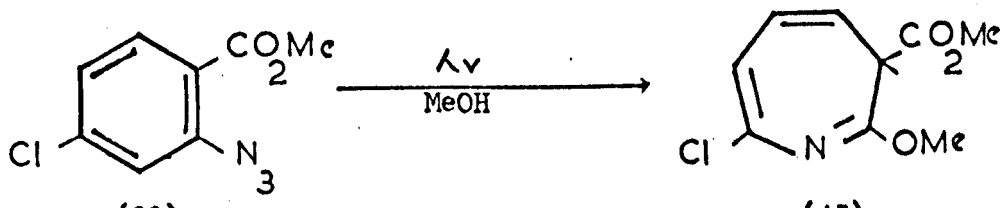
41. R = butyl

These azepines were fully characterised by analytical, spectroscopic (infrared and mass), and ^{1}H nuclear magnetic resonance data. In fact the latter once again proved the most informative in elucidating the structure of these 3H-azepines. For example, 2-methoxy-3-methoxycarbonyl-3H-azepine showed two OMe resonances at τ6.2 and 6.3 respectively with the former more downfield due to the deshielding effect of the carbonyl function. A doublet at τ7.1 is assigned to the 3-proton ($J_{3,4}$ 6.2Hz). The olefinic protons appear at τ3.6-4.5 and a low field doublet is attributable to H-7 ($J_{6,7}$ 7.5Hz). However the nuclear magnetic resonance spectra of these 3H-azepines will be discussed more fully at the end of this section. The phenyl-ester (26) on photolysis in methanol yielded the 2-methoxy-3H-azepine (42).



(26) (42)

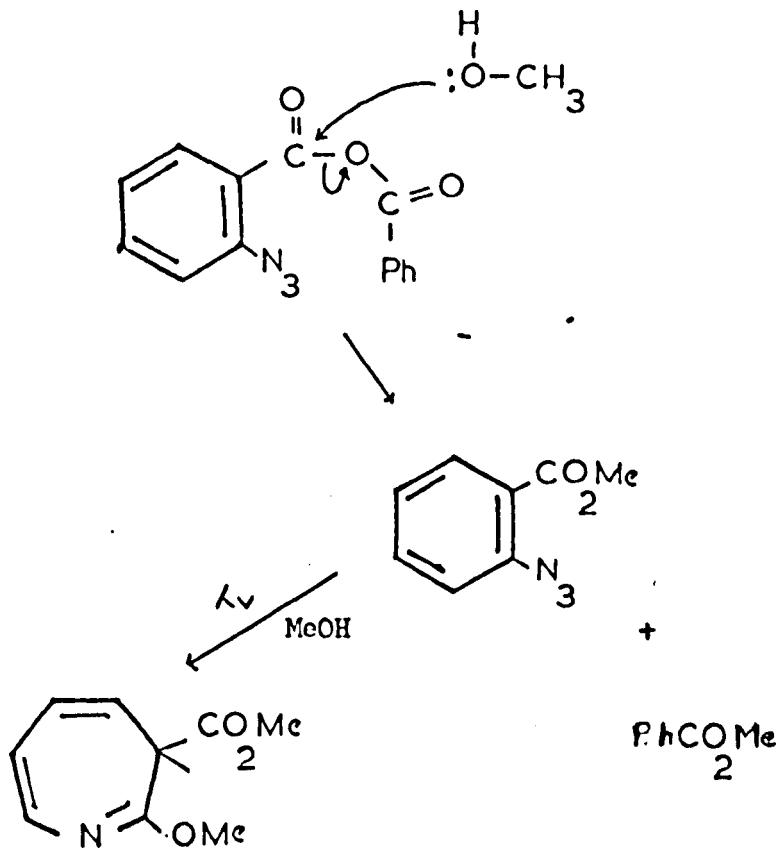
This process appears to be adaptable to the synthesis of further substituted azepines in that photolysis of the chloro-azido ester (22) in methanol proceeded smoothly to give 7-chloro-2-methoxy-3-methoxycarbonyl-3H-azepine (43) in good yield.



(22) (43)

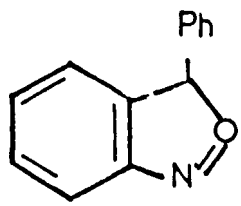
The azidophenylthioester (27) was also photolysed in methanol with the hope of obtaining the 2-methoxy-3H-azepine-3-phenylthioester. However, this reaction resembled the thermolysis result in that only diphenyl disulphide was formed together with intractable tars. The photolysis of o-azidobenzoic acid (5) and 5-azido-2-chlorobenzoic acid (13) in methanol, unlike the esters and amides already discussed, gave only polymeric materials. o-Azidobenzoic anhydride (28) on photolysis in methanol gave as expected 2-methoxy-3-methoxycarbonyl-3H-azepine (37) and methyl benzoate. Predictably the anhydride undergoes methanolysis, probably during photolysis, so that the product is the same as that from the photolysis of methyl o-azidobenzoate. The mode of cleavage of the unsymmetrical anhydride is not surprising on the basis of the known electronic effects of an azido group [121] which will tend to promote nucleophilic attack by the methanol at the o-azidobenzoyl group rather than at the benzoyl group - see Scheme 7. This mode of cleavage was confirmed by stirring the o-azido-anhydride with cold methanol. The reaction was monitored by thin layer chromatography and the anhydride was found to undergo slow methanolysis to yield predominantly methyl o-azidobenzate. Photolysis of 2-azidobenzoyl chloride in methanol was not attempted for the above reasons.

SCHEME 7

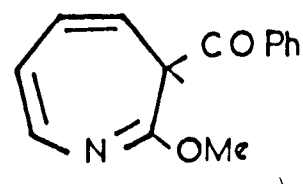


Confirmation of this mode of cleavage of the anhydride was also illustrated by reacting the azidoanhydride with concentrated ammonia, whereupon 2-azidobenzamide was found to be the only amide formed.

2-azidobenzophenone (29) was photolysed in methanol for twenty-four hours to give a mixture of 3-phenylanthranil (44) and 3-benzoyl-2-methoxy-3H-azepine (45).



(44)



(45)

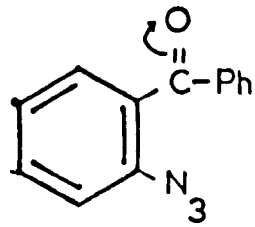
f) Discussion of Results

The formation of azepines from azides under photolytic and thermolytic conditions is well documented [6,7] (also see introduction). In all cases the azepines appear to arise via the singlet nitrene - azirine system, which on reaction with a nucleophile, generally an amine, followed by ring expansion, yields a seven membered ring.

In order to explain why azepines are formed from the azido-amides, esters, ketones and not from azido-acids we made use of results from a recent paper of Dyall and Kemp. [96] These workers investigated the neighbouring group participation of several o-substituted aryl azides. One of the groups thoroughly investigated was the azido substituted carbonyl compounds. From the kinetic data, the activation energy for the pyrolysis of 2-benzoyl, and 2-acetylphenyl azide were found to be 25.8 and 27.2 kCal - mole $^{-1}$ respectively, which is somewhat lower than the activation energies normally associated with a nitrene involvement.

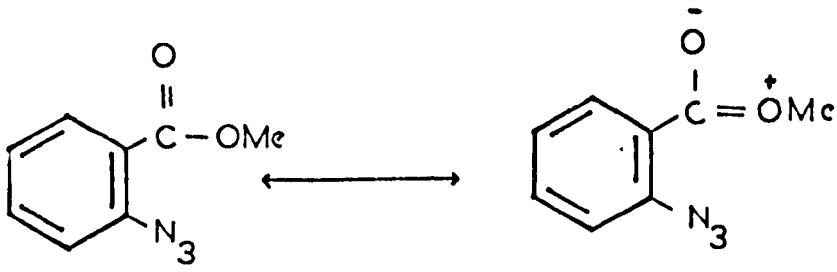
From this they concluded that the ortho ketone group is in some way assisting in the decomposition of the azides. They also indicated that strain within the cyclic intermediate leading to the formation of the new heterocycle, together with the delocalisation energy, are important factors in these azide decompositions. Using these arguments they showed why certain groups (i.e. methoxycarbonyl) will be less effective than for example benzoyl as a neighbouring group.

There is no doubt that the photolysis of 2-azidobenzophenone goes via azide-anthranil-azepine route. These findings have been substantiated by Berwick [15] who photolysed 2-azidoacetophenone and 2-methylanthranil in methanol and in each case obtained 2-methoxy-3-acetyl-3H-azepines. In view of the findings of Dyall and Kemp [96] it can be suggested that the formation of 2-phenylanthranil from 2-azidobenzophenone is an assisted process owing to the fact that a substantial internal resonance energy is lost due to delocalization within the molecule.



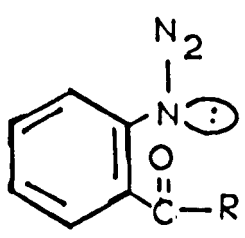
Consequently if the molecule is to react it has to be assisted and probably occurs by way of a 1,3 dipolar addition - a mechanism postulated earlier by Smith and his co-workers. [12] However, on irradiation of the anthranil, cleavage of the N-O bond takes place which results in the formation of a nitrene which can bite into itself to form a relatively stable azirine, and which is attacked by the solvent, followed by ring expansion to give the 2-benzoyl-3H-azepine. This suggestion in fact has been substantiated by the work of Ogata, Kano and Matsomoto [14] who showed that irradiation of 2-phenylanthranil in methanol does lead to the formation of 3-benzoyl-2-methoxy-3H-azepine via a stable azirine species.

With the azido-esters, we find that anthranils are not formed. Instead, the 3H-azepines-3-carboxylates are formed directly. This agrees with the conclusions reached by Dyall and Kemp [96] and indicates that the photolyses are proceeding via a nitrene mechanism.

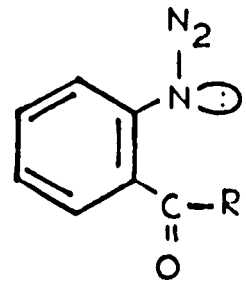


(15)

In the azido-ester (15) the internal resonance energy due to delocalisation is high and consequently the decomposition is not assisted, since this would involve substantial loss of this resonance energy. Hence, decomposition follows a nitrene pathway. The driving force [96] behind these reactions can also be shown to reflect steric acceleration in some azides. Where the ortho-substituent is a carbonyl group (i.e. COR) it can give rise to two conformations with respect to the azido group i.e. 46 and 47.



(46)

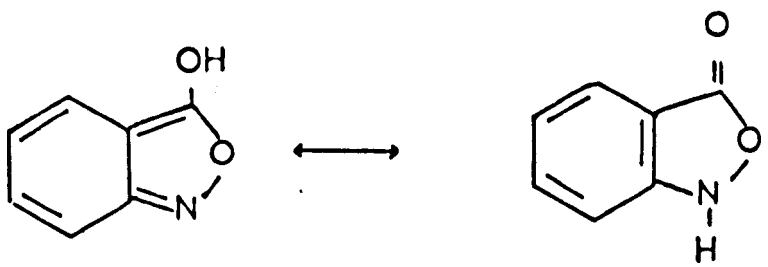


(47)

The conformer (46) involves lone-pair repulsions which are not present in (47), for some identities of the group R. When (R = OMe) both conformers have been shown to exist. Evidence for this comes from the infrared spectrum of the azido-ester which when measured at high resolution, shows two carbonyl peaks ν(CO) at 1736 and 1726 cm^{-1}. However, from the product obtained from the photolysis of this azido-ester, we can predict that the conformer (46) is heavily favoured over that of (47).

A similar explanation could be suggested for the formation of the 3H-azepine-3H-carboxyanilides in terms of the delocalisation energy (i.e. the reactions proceeding via a nitrene mechanism). However, the feature which is baffling is that no azepines or anthranils are formed from the azido-acids. Like the azido-esters and amides, a nitrene mechanism is favoured as the internal resonance energy of the carboxylic acid due to delocalisation is again large.

It is of interest that the product of an assisted decomposition would be the hydroxyanthranil (48) which is a tautomer of the known stable [130] isoxazolane (49).



(48) (49)

However no such product could be detected. A possible explanation for the lack of isolable products from the decomposition of o-azidobenzoic acid may lie in the fact that this acid is a strong acid (p.Ka 29.5 x 10^{-6} in aqueous methanol at 25°) [122] due to the electron withdrawing effect of the azido group. Sundberg and Sloan [131] have shown that the photolysis of aryl azides in mesityline leads mainly to substantial amounts of the 2-mesityl-3H-azepines. However the introduction of 5% acetic acid to the photolysis changes the course of the reaction in that substantial amounts of diphenylamines are produced and only traces of the 3H-azepines are found and the amines are derived from electrophilic substitution of the mesitylene.

Alternatively the o-azidobenzoic acid, particularly on thermolysis, may be undergoing decarboxylation to give phenyl nitrene which, as has been established, in inert solvents yields mainly triplet products and tars.

In an attempt to show that the acidity of the o-azido acid is the main cause of tar formation the acid was converted to its sodium salt. However serious problems were encountered on attempting to photolyse this salt in that it was insoluble in pure methanol and only sparingly soluble in aqueous 50% methanol. Consequently irradiation of the mixture for twenty-four hours was not successful and gave only starting materials.

Azepine formation has been postulated to arise via a singlet nitrene, which is probably in equilibrium with the azirine species. The presence of what was thought to be an azirine species during the formation of 3-benzoyl-2-methoxy-3H-azepine from the photolysis of 2-phenylanthranil in methanol was clearly demonstrated

by Ogata and his co-workers.[14] These authors monitored the disappearance of the anthranil in cyclohexane, and the appearance of a species, thought to be the azirine, by means of ultra violet spectroscopy. On addition of methanol to the irradiated solution, ultra violet measurements showed the disappearance of the intermediate species and the formation of the azepine.

In view of this result, we photolysed methyl o-azidobenzoate in dichloromethane,[132] a well known singlet sensitiser and followed the reaction on an ultra violet spectrometer. In this experiment a 0.2% azide solution was employed and a varied ultra violet absorption curve was obtained (i.e. Figs. 1-3). The absorption curve changed upon the addition of methanol in the dark (Fig. 3). These recordings were taken on the spectrometer with a few drops of spectroscopic cyclohexane added due to the fact that the lower absorption of dichloromethane appears at wavelength 225 n.m. In fact a relatively stable azirine species was shown to exist as indicated by the U.V. absorption curve. However attempts to isolate the "so-called species" without the addition of methanol gave polymers.

Since 3H-azepines are thought to arise via a singlet nitrene, the yield of the azepine should decrease in carrying out the photolysis in the presence of a triplet sensitiser. Accordingly methyl o-azidobenzoate was photolysed in a mixture of methanol and acetophenone, a well known triplet sensitiser.[133] The results were as predicted in that the 3H-azepine was obtained in much reduced yield (10%), whereas methyl anthranilate, a triplet based product was obtained in a 40% yield. This supports the idea that the

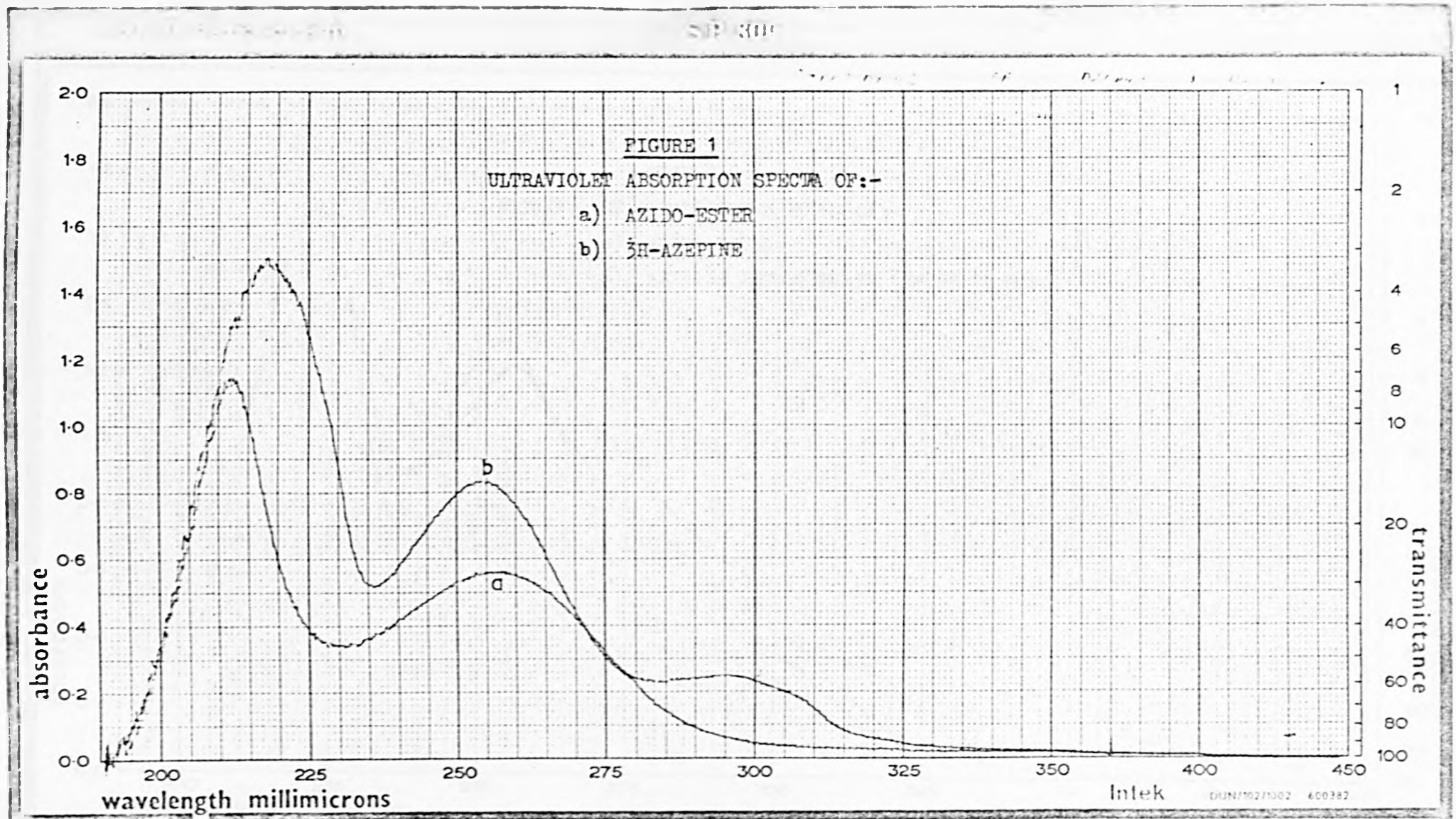
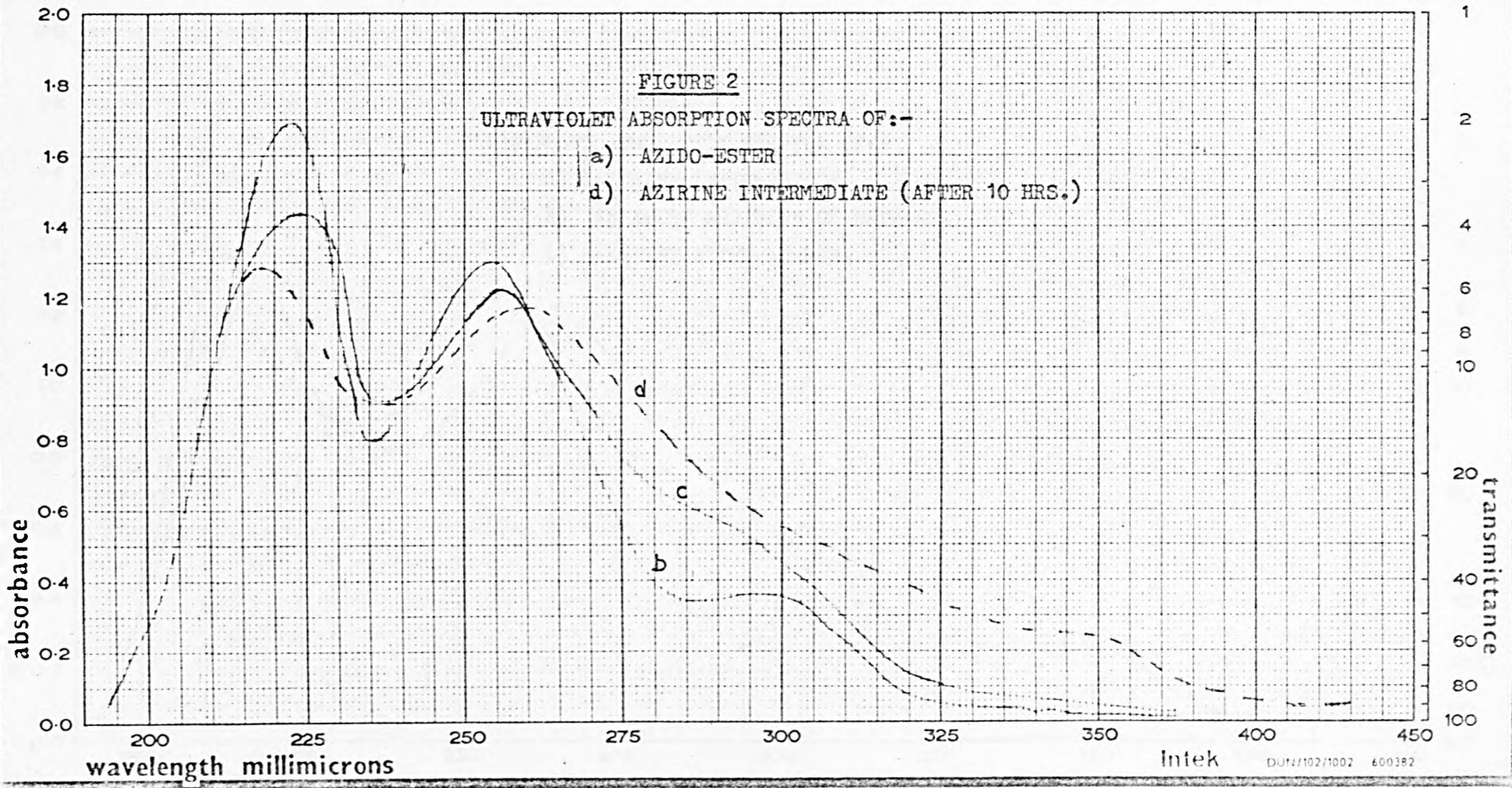


FIGURE 1
ULTRAVIOLET ABSORPTION SPECTRA OF:-
a) AZIDO-ESTER
b) 3H-AZEPINE
absorbance
transmittance
wavelength millimicrons
2·0
1·8
1·6
1·4
1·2
1·0
0·8
0·6
0·4
0·2
0·0
1
2
4
6
8
10
20
40
60
80
100
200
225
250
275
300
325
350
400
450
b
a
Intek
ALIGN WITH INDEX ON THE RECORDER
SAMPLE AND FORMULA
CONCENTRATION
REFERENCE
PATH LENGTH
SCANSPEED FAST
SLOW
DATE
OPERATOR
REF NO

SP 800



ALIGN WITH INDEX ON THE RECORDER

SAMPLE AND FORMULA

CONCENTRATION

REFERENCE

PATH LENGTH MM

SCAN SPEED FAST ☐ SLOW ☐

DATE

OPERATOR

REF NO.

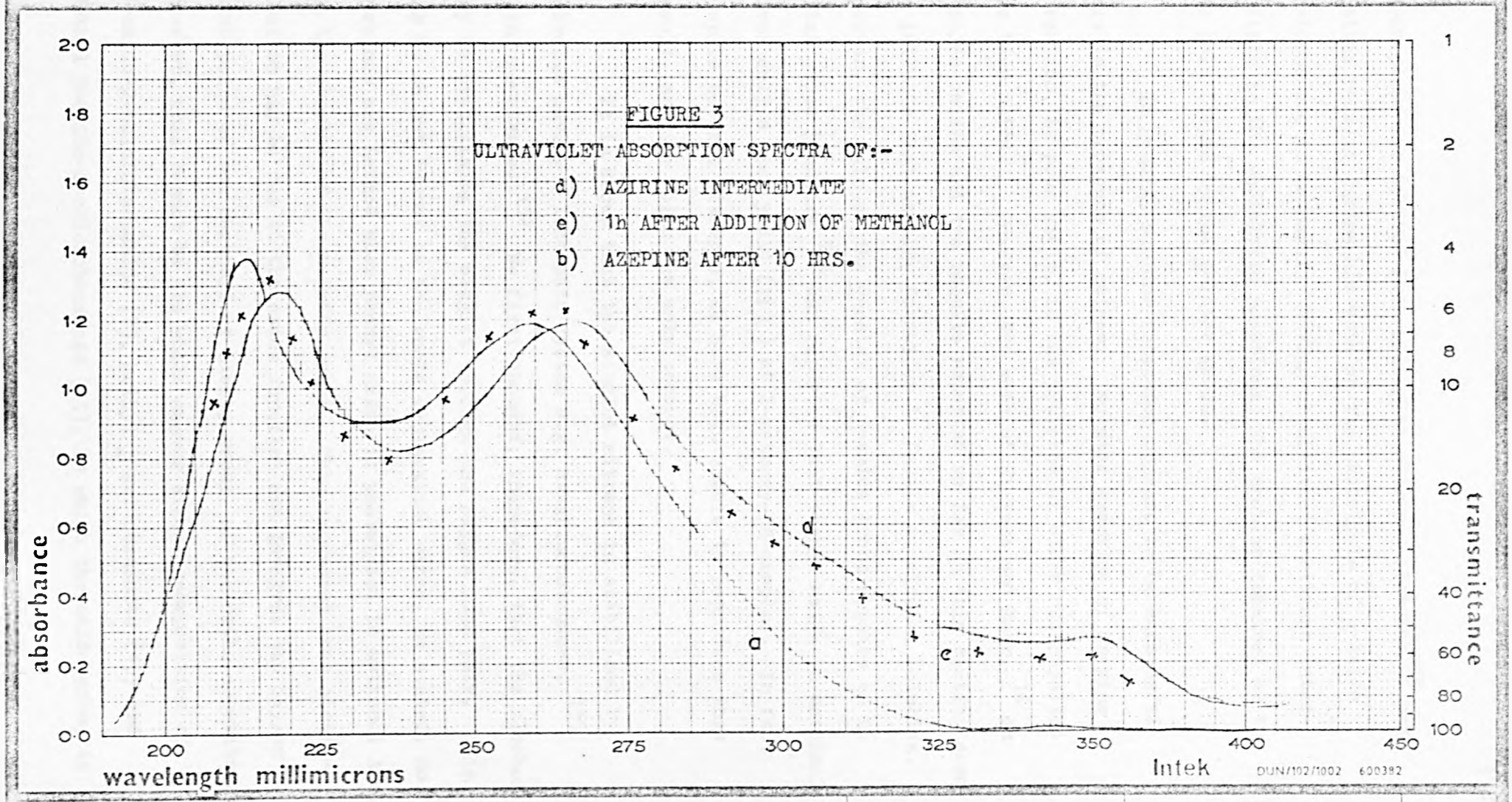


FIGURE 3

ULTRAVIOLET ABSORPTION SPECTRA OF:-

d) AZIRINE INTERMEDIATE

e) 1h AFTER ADDITION OF METHANOL

b) AZEPINE AFTER 10 HRS.

ALIGN WITH INDEX ON THE RECORDER

SAMPLE AND FORMULA

CONCENTRATION

REFERENCE

PATH LENGTH MM

SCAN SPEED FAST ☐ SLOW ☐

DATE

OPERATOR

REF. NO

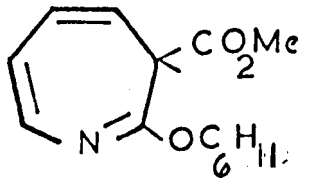
3H-azepines are derived from a singlet nitrene. Berwick [15] had similar results during his work on the photolysis of o-azido acetophenone in methanol. Having established a nitrene intermediate in the photolytic reactions, the problem remained as to the role played by the o-ester group.

In general azepine formation appears to be successful only in the presence of amines. Isolated examples of azepine formation, in poor yield, in the presence of other nucleophiles has been noted.[7] However, the work of Stevens and Mair, [16] on o-azido-amides and the results reported so far in this section seem to indicate that azepine formation is facile in alcohol solution. However, the role of the o-ester or o-amide group appears to be vital since Sundberg [134] has reported that phenyl azide in methanol gives only a poor yield (11%) of 2-methoxy-3H-azepine. In fact despite several attempts, we have been unable to reproduce this result, aniline being the only product.

It is known that the singlet nitrene is stabilised by solvents having a lone pair system e.g. hexafluorobenzene, [135] dichloromethane. [132] We first thought, therefore, that the alcohol may be stabilising the singlet through the oxygen lone pair. This may be so but cannot be the whole explanation since, as stated, no azepines are formed when phenyl azide is photolysed in methanol i.e. in the absence of the o-ester group. This suggested that stabilisation may be due to the ester function and involves the oxygen lone pairs of the carbonyl or alkoxy group of the ortho substituent. However, this cannot be the whole answer since decomposition of 5-azido-2-chlorobenzamide (8), methyl p-azidobenzoate (19) and methyl 5-azido-2-chlorobenzoate (13), in which the azido group is

meta- or para- to the ester or amide function gave mainly amines i.e. triplet based products, and no 3H-azepines when photolysed in methanol solution. It is interesting to note that Cadogan and his co-workers [136] obtained 3H-azepines on heating o-, m-, and p-nitrobenzoate esters with triethyl phosphite in the presence of diethylamine.

We suggest, therefore, that perhaps the singlet nitrene is being stabilized by a combination of intra and intermolecular interactions with the ester oxygen lone pairs and with the lone pair of the solvent. On this assumption we could see no reason why the o-azido-esters should not decompose thermally in a suitable alcohol to give 2-alkoxy-3H-azepines. Cyclohexanol (b.p 160°) appeared to be a medium of suitable boiling point, as predicted methyl o-azidobenzoate decomposed in the alcohol at 140° to give 2-cyclohexyloxy-3-methoxy carbonyl-3H-azepine (50) in 20% yield and methyl anthranilate (60%).

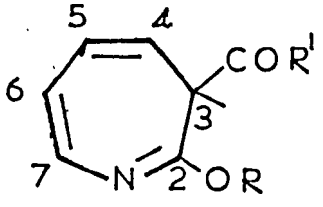
(50) 

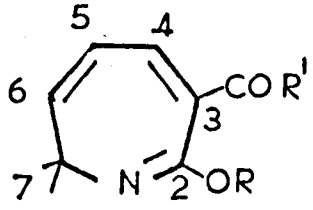
Significantly phenyl azide decomposed in boiling cyclohexanol to gave predominantly triplet based products i.e. azobenzene and aniline. Attempts to extend this thermolytic reaction to include phenols failed, in that decomposition of methyl o-azido-benzoate in m-cresol gave methyl anthranilate (10%) plus tars. Possibly this is due to the acidic nature of the phenol, a factor which as already discussed, does not favour azepine formation.

g) <u>^{1}H Nuclear Magnetic Resonance Spectra of the 3H-azepines</u>

The nuclear magnetic resonance spectra of 3H-azepines formed from the photolytic decompositions of the o-azido-carbonyl compounds show similar features to the 3H-azepines from the thermolysis of aryl azides in primary and secondary amines, and to the 2-alkoxy-3H-azepine-3-carboxamides prepared by Stevens and Mair.[16]

It is worth noting that during the discussion all the azepines have been rationalized to be the 3H-isomers when in fact the 7H-isomers are a possibility, as shown by the diagram below.





a) R^1 = OMe R = Me

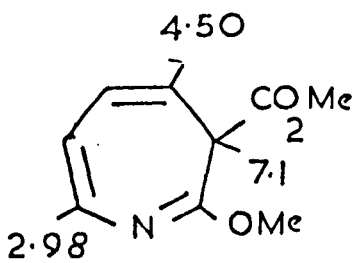
b) R^1 NH_2 R = Et

c) R^1 = Ph R = Me

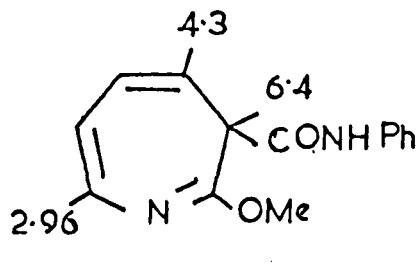
Both structures contain the system

C-(7H) = C-(6H)- C(5H) = C(4H) and should give rise to one doublet due to the proton at position 7, no triplet in the olefinic region, and a simple doublet between τ(5-6) due to the allylic hydrogen atoms. Our preference for the 3H-isomers over that of the 7H-isomers is based on that of chemical shift differences and these follow from arguments developed by Vogel and Erb, [137] in their establishment of the structure of 1,2-dihydro-2-keto-3H-azepine.

If the 7H-isomer was the correct structure then the proton at position (7H) would be α to the amidine carbon atom whereas proton (6H) would be β to this centre. In α, βunsaturated carbonyl compounds and nitriles, the hydrogen is always shifted to a lower field than the α-hydrogen atom and assuming, not unreasonably, that the amidine function is electronically similar to these groups, then in the 7H-isomer we would expect to find the proton at carbon (6) to be shifted to a lower field than that associated with carbon (7) which is not the case.



(37)



(32)

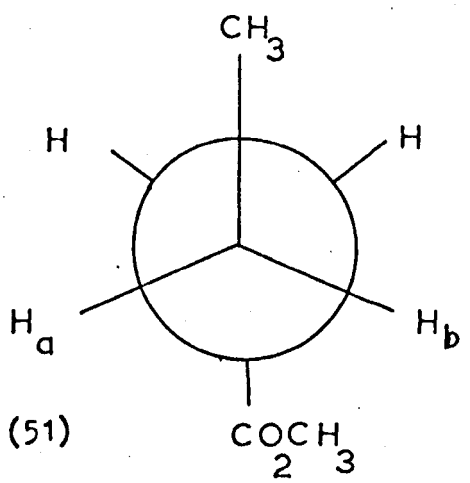
Similarly double bonds attached to atoms with unshared electrons, i.e. α-hydrogens, should appear at lower field. [138] Examples are α-hydrogen (1.50) and β-hydrogen (3.02) in pyridine, [138] α-(2.60) and β-(3.70) in furan. [138] By analogy the proton at position 7 in the ring should be shifted further downfield if it were the 3H-structure than it would be in the 7-H isomer. This is in fact what is observed in all cases, again indicating that the 3H-isomer is the more consistent of the two isomers on the basis of ^{1}H n.m.r.evidence.

The azepines (37) and (32) used to illustrate these features were obtained by photolysis of methyl o-azidobenzoate and N-(o-azidobenzoyl)aniline in methanol.

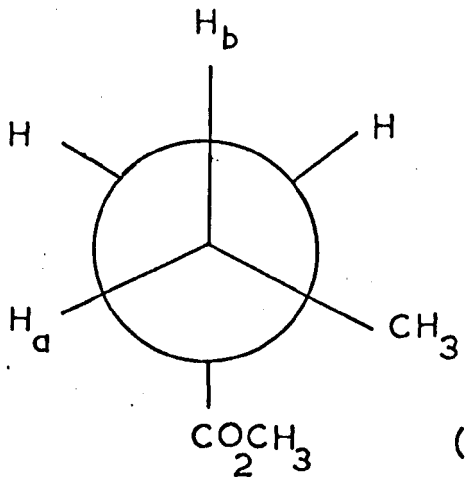
The protons at position 7 in both structures appear at τ 2.98 and 2.96 respectively; whereas the protons at position 3 appear at τ 7.1 and 6.4. The lower value of the latter is attributable to a more electronegative environment of this proton together with the anisotropy of the benzene ring which causes a greater deshielding of the 3H-proton so that at resonates further downfield. Additional interesting features are visible in the spectra of 2-ethoxy-(38), 2-(n-propoxy) (39), and 2-(n-butoxy) (41) 3H-azepine.

For example, instead of the simple four line pattern of the A part of an A_2X_2 system which is normally associated with ethyl groups, in the case of the 2-ethoxy compound (38), a complicated spectra is observed in that the $-O-CH_2$ group appears as an octet, i.e. A B C_3 pattern. This can be explained in terms of the asymmetric centre at C-3 and a magnetic non-equivalence

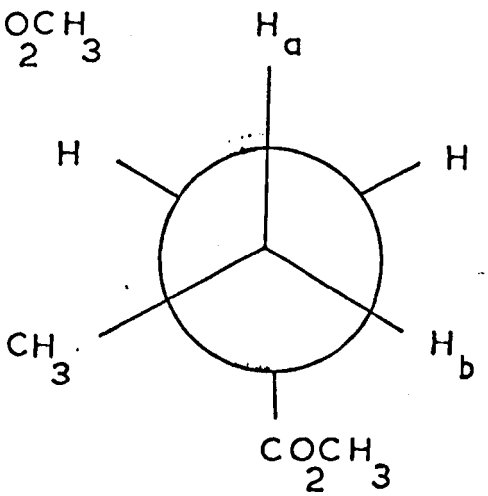
which arises from the location of the methylene group in this asymmetric environment. In such systems, apart from the intrinsic asymmetry which causes the observed non-equivalence of the methylene protons, it has been suggested [139] that the chemical shifts between the two methylene protons arise from unequal populations of the rotational conformers shown below.



(51)



(52)



(53)

This pattern is well documented and several similar examples are known.[139,140,141,142] A similar argument can be used to explain the septet observed for the O-CH_2 proton of 2-(n-propoxy)azepine (39) and the multiplicity shown by the (O-CH_2) protons in the 2(n-butoxy) azepine (41).

Another interesting feature comes from the spectra of the 2-(isopropoxy) azepine (40) as shown in diagram (4). There again the non-equivalence of the two methyl groups can be explained in terms of their proximity to an asymetric centre. There instead of the expected octet i.e. an A B C_3 pattern, a simple AB - type ^1H n.m.r.spectra is observed and this feature has been well documented by Roberts and his co-workers [143] for an isoproyl group associated with an aromatic ring via an asymmetric centre. They indicated that the principal contributors to the non-equivalence of the methyl protons originate in the magnetic anisotropy of the benzene ring. We however do not have such a system and therefore the principal attributors to this non-equivalence of the methyl protons must arise from its proximity to the asymmetric centre at C_3. Finally it must be pointed out that in all the 3H-azepines synthesised, there is an asymetric carbon centre at position 3, and on this basis the azepines should be resolvable into two enantiomeric forms. However, lack of time prevented any attempts at this separation.

h) Mass Spectra of 2-Alkoxy-3H-azepines

The mass spectral breakdown patterns of azepines are not well documented. 1H-Azepines undergo fragmentation of the ring nitrogen atom and the 1H-substituent bond to give an azatropylium cation (54) (m/e 92) as the base peak. Stevens and Mair [16] found that

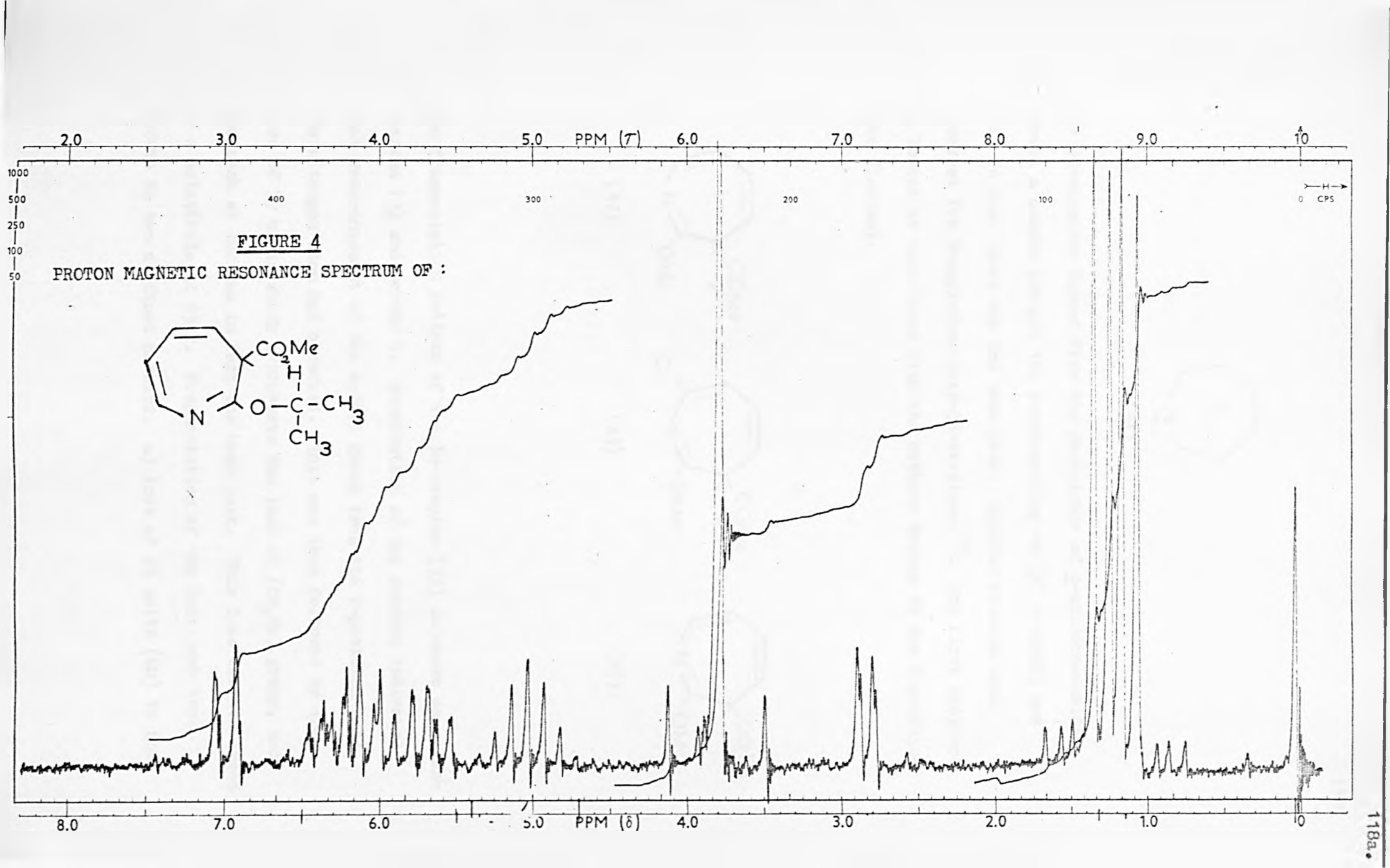
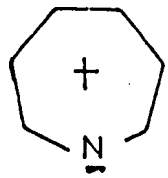


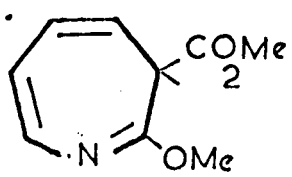
FIGURE 4

PROTON MAGNETIC RESONANCE SPECTRUM OF :

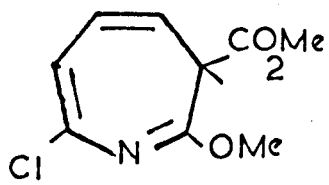


(54)

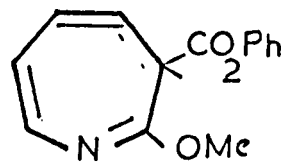
the 3H-azepines formed from the photolysis of o-azidobenzamides, showed a common ion m/e 122 corresponding to (M^+ - CONHR) and this in some cases was the base peak. Similar results were observed for 3-acyl-2-methoxy-3H-azepines [14]. The first azepines we looked at were those with the methoxy groups in the 2-position (see diagram).



(37)



(43)

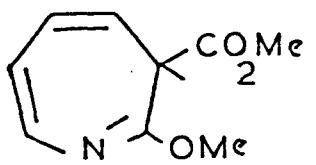


(42)

The fragmentation pattern of the 3H-azepine (37) is shown as a line diagram (5) and Scheme 8. Examination of the spectra indicated that rearrangement of the methyl group from the 2-position onto the nitrogen atom had occurred. This was then followed by the loss of 59 units which represents the loss of (CO_2Me) group, and the peak at 122 was in fact the base peak. This loss was confirmed by a metastable at 83.2. Fragmentation of the base peak then occurs in two distinct manners. a) loss of 28 units (CO) to form

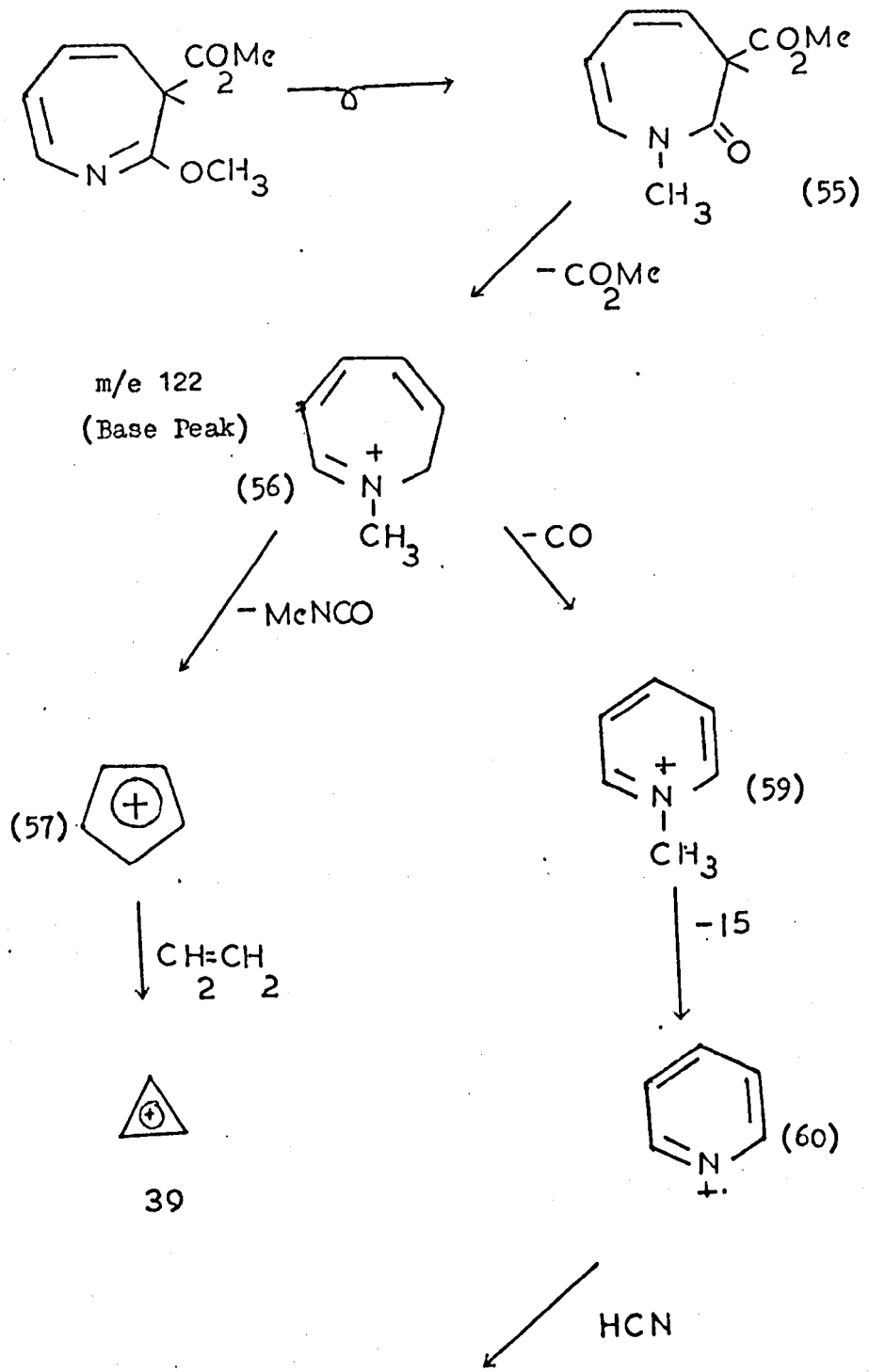
FIGURE 5

Mass Spectrum of :



metastables at 83.2 and 72.4

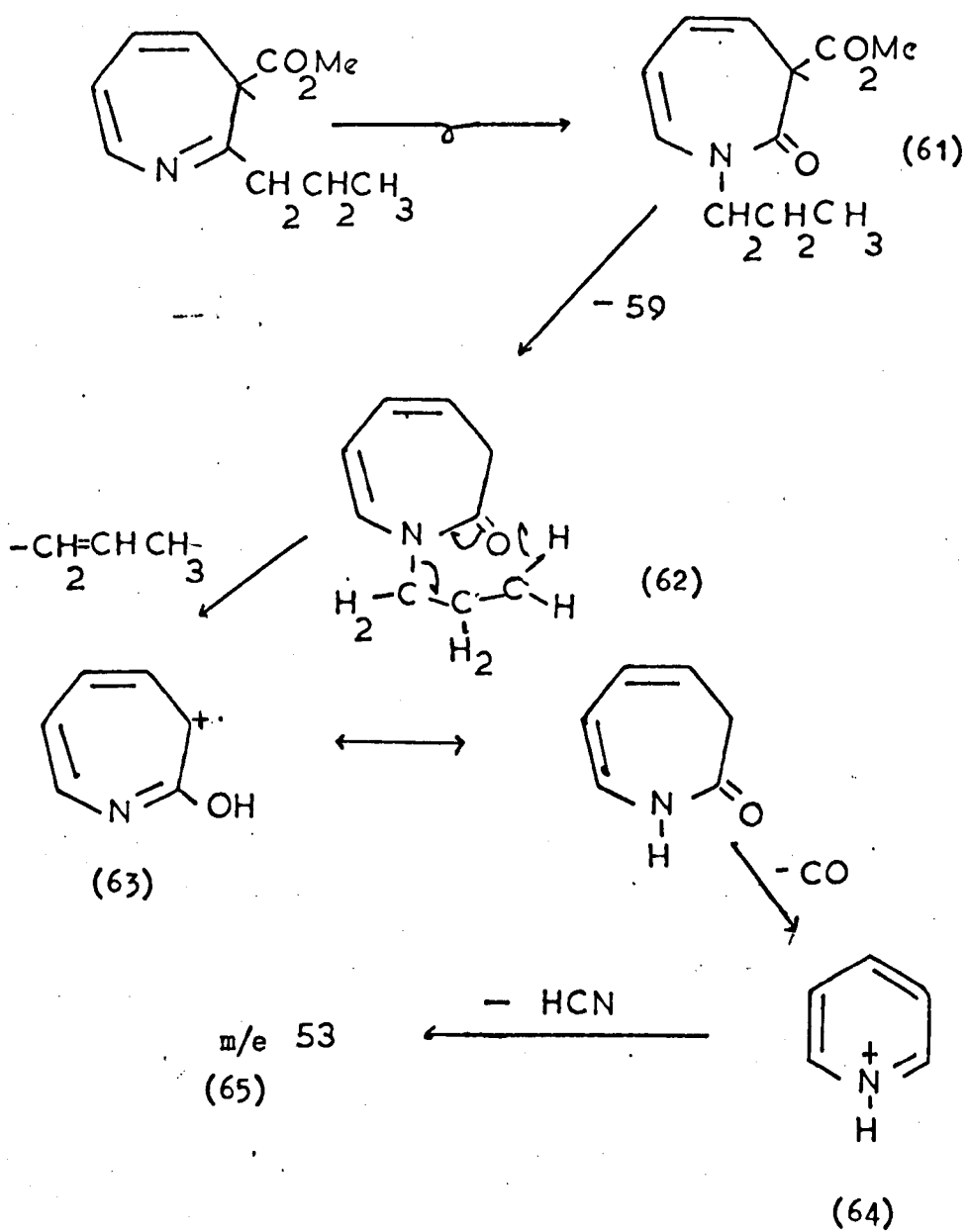
SCHEME 8


COMe2
OCH3
N
CO2Me
O
N
CH3
(55)
-CO2Me
m/e 122
(Base Peak)
(56)
N
CH3
-MeNCO
-CO
(57)
CH=CH2
2
2
39
(59)
N
CH3
-15
(60)
N
HCN
m/e 52
(61)

the m/e 94 fragment (confirmed by metastable at 72.4), and (b) loss of 57 units (MeNCO) to form the cyclopentadienyl cation (57), which decomposes further with the loss of acetylene to yield the cyclopropenium cation (58). The N-methyl pyridinium cation (59) may decompose to the pyridinium cation (60) with the loss of 15 units, which in turn breaks down to give the species (61) (m/e = 52) with the loss of hydrogen cyanide. This fragmentation pattern is also shown by the 7-chloro azepine (43) and the phenyl-ester (42). Both had base peaks at m/e 122, in the latter case resulting from the loss of 121 units ($PhCO_2$), and the former by the loss of 94 units (Cl + CO_2 Me). The important feature concerning these fragmentations is that unlike that of the 1H-azepines the azatropilium cation is absent. Another minor fragmentation of these 2-methoxy-3H-azepines includes the loss of methanol, which is analogous to 1-carbemethoxy-1H-azepines bearing methyl groups at the 2-, 3-, and 4 position.[144] Similar fragmentation patterns were also obtained for 3-benzoyl-2-methoxy--3H-azepine which indicates that 3H-azepines with a carbonyl group in the 3-position and a methoxy group in the 2-position follow the same fragmentation pattern. However, when the 2-alkoxy group in the 3H-azepine system is longer than (OEt) a different fragmentation pattern is observed and this feature can be illustrated with reference to 3-methoxycarbonyl-2-(n-propoxy)-3H-azepine. The base peak is no longer (M^+ -59) units but (M^+ - 59+42) = 108 which arises by way of a McLafferty rearrangement as shown in Scheme 9. As reported for the previous fragmentations rearrangement of the n-propoxy group to give the structure (61) may occur. This rearranged product then loses 59 units to give the fragment (62).

This loss is supported by the metastable at 107.6. This ion then looses 42 units to give the base peak at 108, again supported by metastable 77.6 and this in turn may then decompose as shown in Scheme 9. In addition to those fragmentations outlined, there are alternative breakdown patterns, i.e an m/e at 91 which indicate the presence of the azatropilium species, but these were not further investigated. The 3H-azepine-3-carboxamides gave similar fragmentation patterns.

SCHEME 9

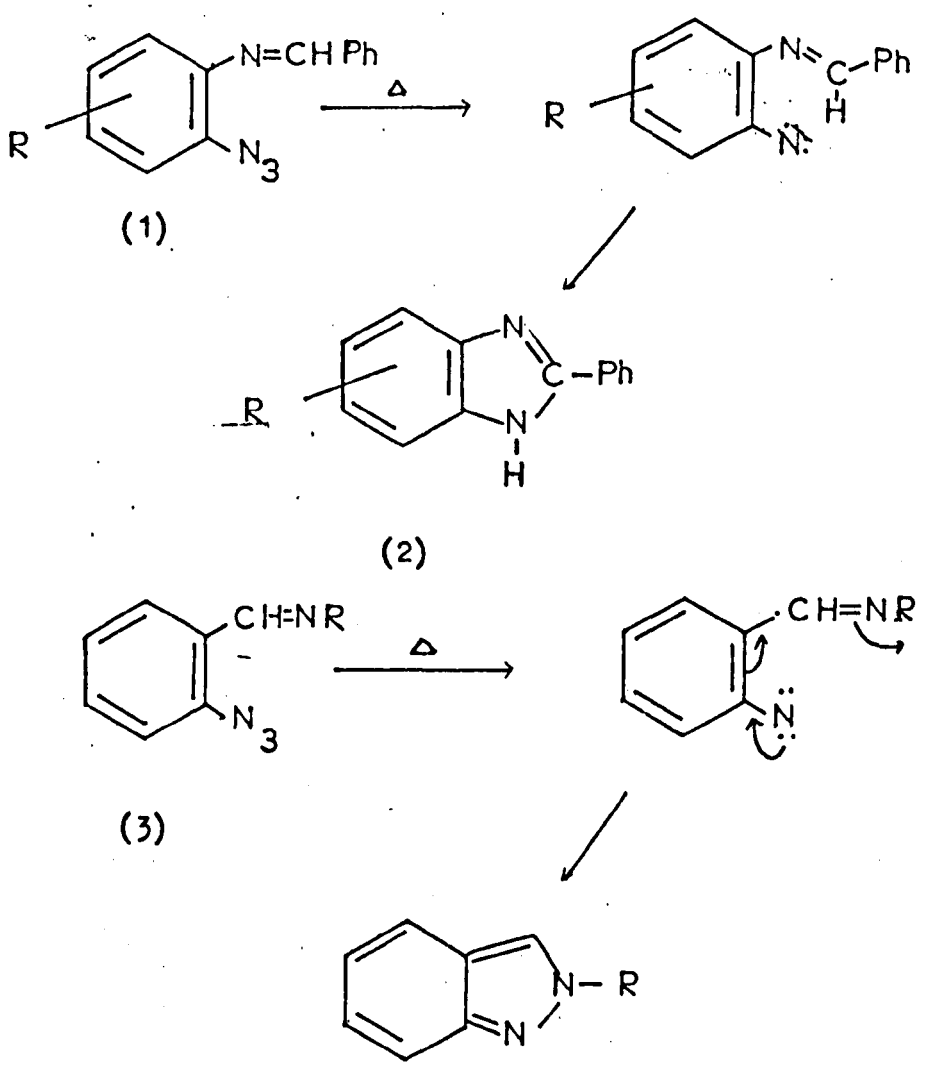


CHAPTER 4

SYNTHESIS AND DECOMPOSITION OF o-AZIDO-AMINO COMPOUNDS AND THEIR DERIVATIVES

The synthesis of o-azidoaniline and a few of its derivatives has been well documented. However, little study appears to have been made on their mode of decomposition. In fact the only reported decompositions [42,118] are the pyrolyses of the anils (1) which gave the benzimidazoles (2) in high yield, and the pyrolyses of the isomeric anils (3) derived from o-azidobenzaldehyde which gave rise to the indazoles (4). Both reactions are summarised in Scheme 1.

SCHEME 1



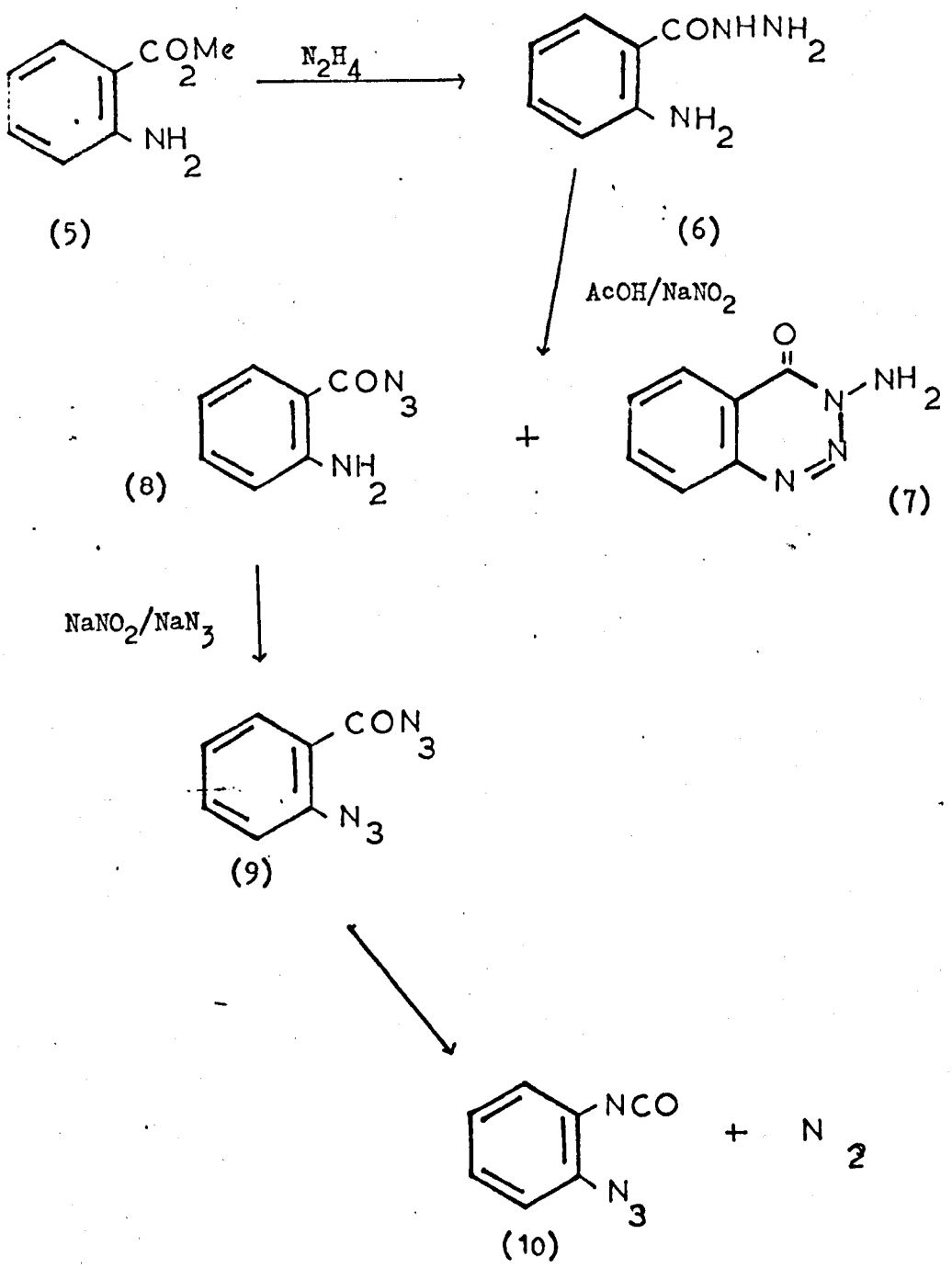
In the previous chapter, we have shown that azides with an ortho electron withdrawing carbonyl group yield mainly polymeric materials on thermolysis, and 3H-azepines on photolysis. On this basis we decided to compare the effect of these ortho electron withdrawing groups with that of the electron donating amino derivatives on the mode of decomposition of aryl azides.

Several o-azidoanilino derivatives have been synthesised namely ureas, carbanates, isocyanate, amides, thiourea, and imide. In all cases the azides were decomposed thermolytically, whereas photolytic decompositions were carried out only on selective examples and these are discussed later.

a) Synthesis of 2-Azidophenyl isocyanate

The synthesis of 2-azidophenyl isocyanate (10) a hitherto unreported compound was achieved by gently heating under reflux at 50° a solution of 2-azidobenzoyl azide (9) in a dry solvent. The expected Curtius rearrangement occurred smoothly to give the isocynate (10) and as predicted no decomposition of the aryl-azido group was experienced at this low temperature. However, synthesis of the isocyanate precursor (9) was difficult and the overall yield was poor due to the fact that o-aminobenzoyl azide, the precursor of the diazide (9), was a minor product from the diazotisation of the o-aminobenzoyl azide (6). The synthesis of the azide (10) is outlined in Scheme 2.

SCHEME 2


COMe
2
NH
2
(5)
N_2H_4
CONHNH
2
NH
2
(6)
AcOH/$NaNO_2$
CON
3
NH
2
(8)
+
O
NH
2
N
N
N
(7)
$NaNO_2/NaN_3$
CON
3
N
3
(9)
NCO
N
3
(10)
+
N
2

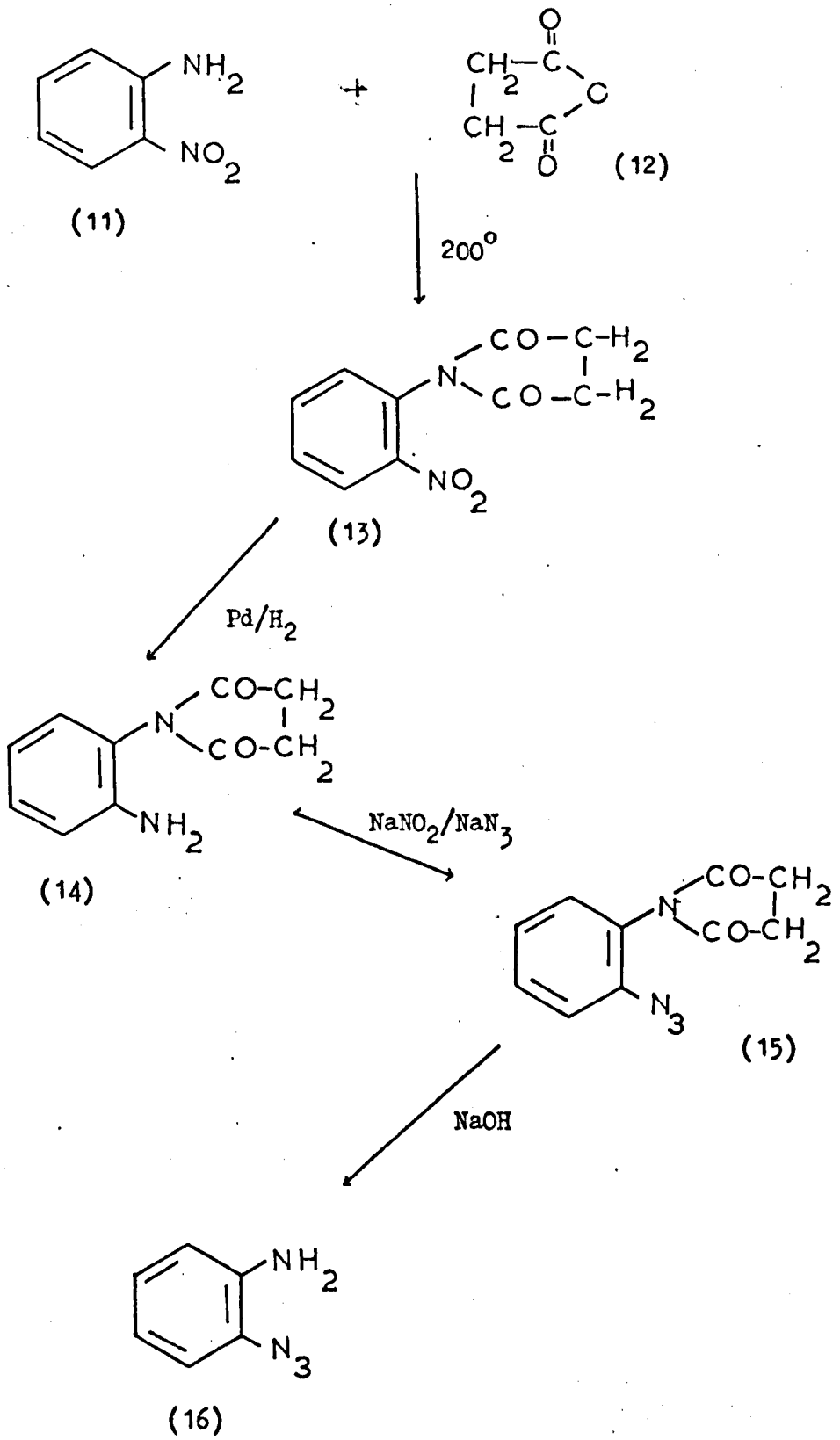
The formation of the 2-aminobenzohydrazide (6) was achieved by treating the amino-ester (5) with hydrazine hydrate in ethanol. The conversion of the hydrazide (6) to the acid-azide (8) by diazotisation in hydrochloric acid was poor and was accompanied by formation of the benzotriazinone (7). However an improved yield was obtained by carrying out the diazotisation in glacial acetic acid.[145]

2-Azidobenzoyl azide (9) was obtained as a white solid m.p. = 28°, the infrared spectrum of which showed a broad absorption band at $\nu(N_3)$ at 2140 cm^{-1} and $\nu(CO)$ at 1730 cm^{-1} consistent with a diazide structure. Mass spectral data showed a molecular ion of 188 mass units, again in agreement with the proposed structure. The o-azido acid azide (9) was somewhat unstable, in that on standing, it rapidly rearranged to give the isocyanate (10) which was identified by the strong isocyanate absorption peak $\nu(2255)$ cm^{-1} in the infrared spectrum. The azido-isocyanate was further characterised by its conversion to the o-azido-urea on treatment with aniline (see later section).

b) Synthesis of o-Azidoaniline

The o-azidoaniline was synthesised by a literature method.[142] The success of this synthesis depends on protecting the amino group while the azido function is being introduced. This was achieved as outlined in reaction Scheme 3.

SCHEME 3

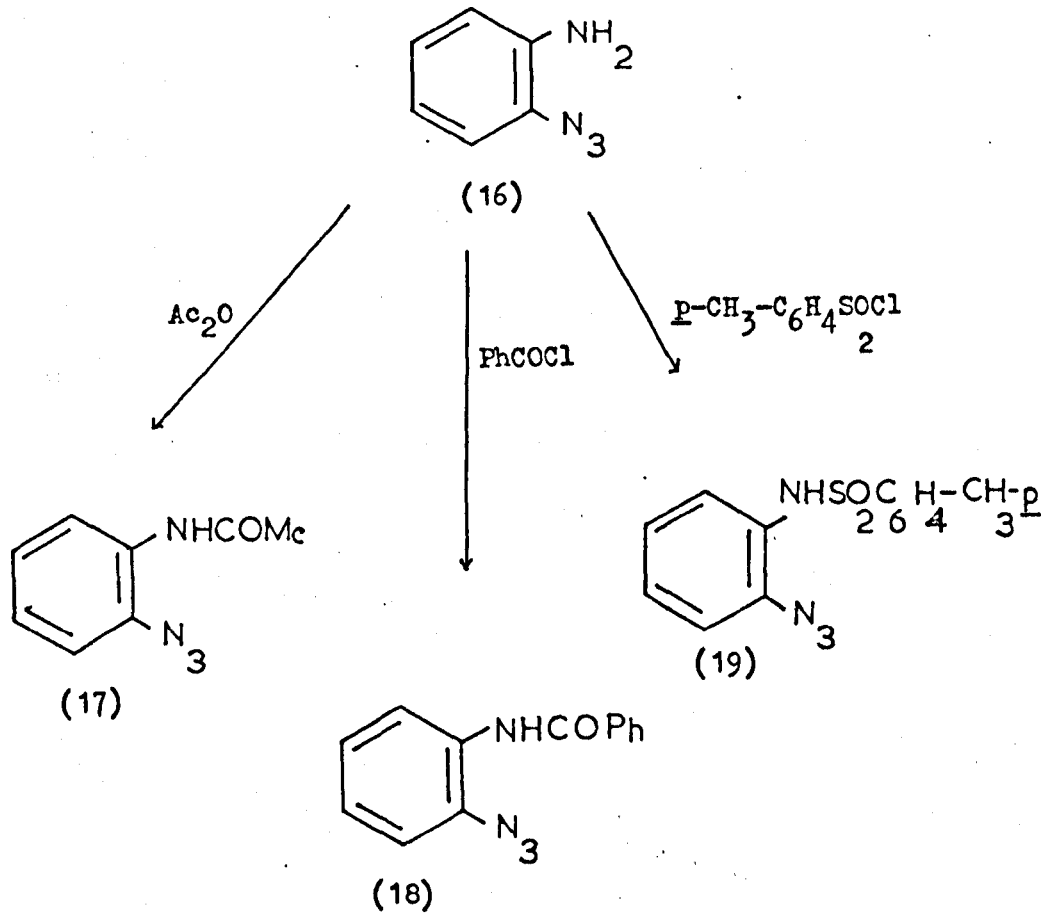

NH2
NO2
(11)
+
CH2—C
CH2—C
O
O
O
(12)
200°
CO—C-H2
N
CO—C-H2
NO2
(13)
Pd/H2
CO-CH2
N
CO-CH2
NH2
(14)
NaNO2/NaN3
CO-CH2
N
CO-CH2
N3
(15)
NaOH
NH2
N3
(16)

The first stage of the synthesis was carried out by the method of Meyer and Maier [146] and this involved heating the nitro-amine (11) with succinic anhydride (12). However, the N-(o-nitrophenyl) succinimide (13) was obtained as a black mass, and repeated crystallisation from ethanol as directed by these workers gave only poor yields of the nitro compound (13). It was found that the impurities could be removed by grinding the dark mass into a powder and then extracting it with an ether-toluene mixture. The residue was then dissolved in hot ethanol, decolourised with charcoal, and allowed to crystallise, whereupon the N-(o-nitrophenyl) succinimide was obtained. The second and third stages of the synthesis were accomplished as indicated in the reaction scheme and the azidosuccinimide (15) on careful hydrolysis with 10% sodium hydroxide solution at 70° gave o-azidoaniline (16) in good yield. Temperature control during the hydrolysis reaction was important since at higher temperatures decomposition of the azide was possible and also the azidoaniline (16) readily sublimes at temperatures around its melting point (63°). This azide was obtained as a white solid which gave identical spectral data to the sample obtained by Smith and Brown. [121]

c) Synthesis of o-Azido-N-substituted Anilines

o-Azidoacetanilide (17) (m.p. = 87°) was obtained by the acetylation of o-azidoaniline with acetic anhydride on a water bath at 100°. o-Azidobenzanilide (18) (m.p. = 86°) was obtained by benzoylation of 2-azidoaniline in pyridine solution, whereas 2-azido-N-(p-tosyl) aniline (19) (m.p. = 130-140°) was prepared by treating p-toluenesulphonyl chloride with o-azidoaniline in pyridine. The reaction Scheme summarising the formation of these azido-amides is shown below.

SCHEME 4



d) o-Azidophenyl ureas

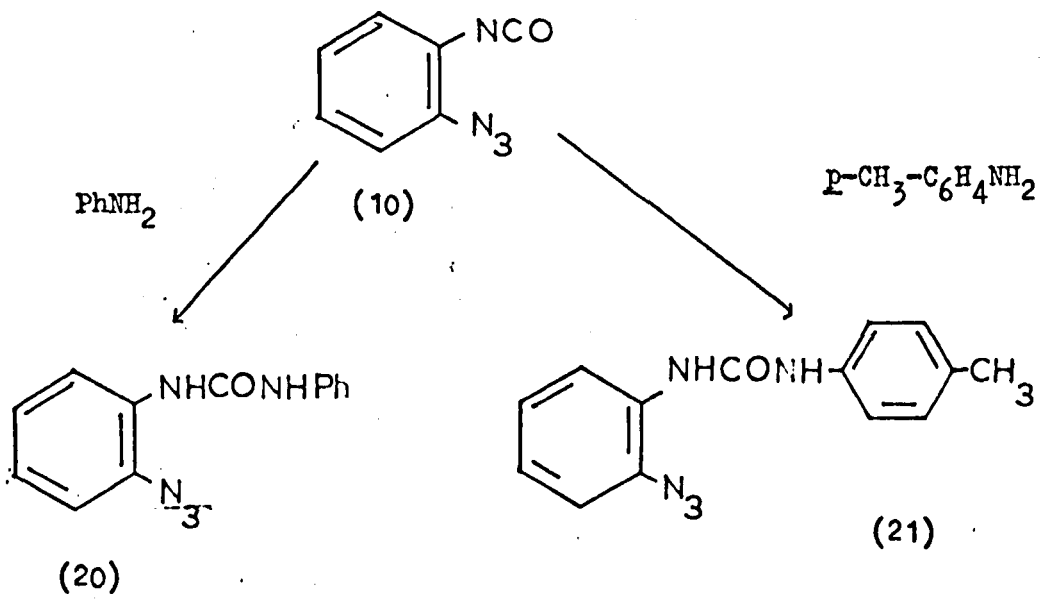
N-Phenyl-N'-(o-azidophenyl)urea (20) was synthesised by reacting aniline with o-azidophenyl isocyanate in light petrol solution. The urea was obtained as a white crystalline solid (m.p. = 174°) and was characterised by analytical and physical data.

Similarly N-(o-azidophenyl)-N'-(p-tolyl)urea (21) was synthesised by reacting p-toluidine with the azidoisocyanate.

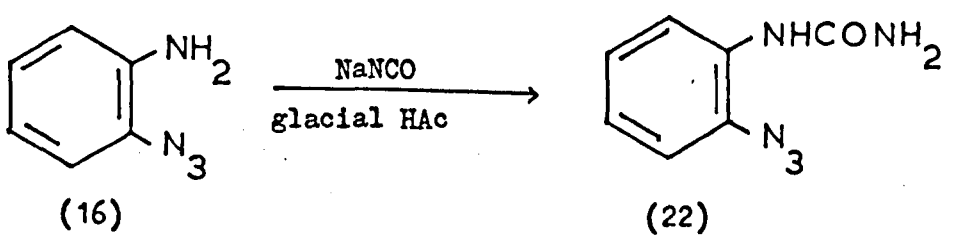
Finally N-(o-azidophenyl)urea (22) was also synthesised but not via the route as shown above but by a Wöhler rearrangement. 2-Azidoaniline in aqueous acetic acid was warmed with sodium cyanate to give the azidourea as a white solid (m.p. 170°) which was again characterised by physical and analytical data.

The syntheses of these azidoureas are summarised in Schemes 5 (a) and (b).

SCHEME 5a

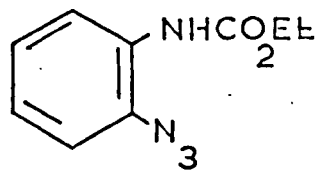


SCHEME 5b



e) Synthesis of Ethyl N-(o-azidophenyl)carbamate

The synthesis of ethyl N-(o-azidophenyl)carbamate (23) was achieved by two methods.

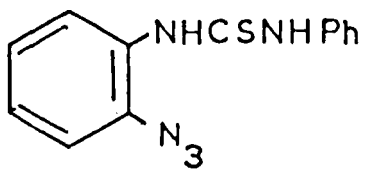


(23)

The first involved heating under reflux a solution of 2-azidobenzoylazide in ethanol. The initially formed isocyanate (obtained via a Curtius rearrangement of the acid azide) reacted with ethanol to give the azidocarbamate (23) in good yield. However, owing to the difficulty in obtaining the acid azide (10) (as mentioned previously in this chapter) an alternate synthesis was employed. This involved reacting 2-azidoaniline with ethyl chloroformate in pyridine solution. In both instances the azide was obtained as a pale yellow liquid which on standing rapidly darkened. However, its structure was once again borne out by physical and analytical data. For example mass spectra showed a mass ion of 190 units and the infrared spectrum showed ν(NH) 3415 cm^{-1}, $\nu(N_3)$ 2120 cm^{-1} and $\nu(N-\overset{O}{\overset{\|}{C}}-O)$ at 1745 cm^{-1}, features consistent with an azidocarbamate. ^{1}H.n.m.r. spectrum in carbon tetrachloride also showed a simple A.B spectrum, i.e. τ(5.8-6.1), a quartet due to CH_2, and τ(8.7-8.9), a triplet due to the CH_3 protons, all of which were in agreement with the proposed structure.

f) Preparation of N-(o-azidophenyl)-N'-phenylthiourea

The synthesis of the azido-thiourea (24) was accomplished by heating under reflux 2-azidoaniline with phenyl isothiocyanate in light petrol solution. The thiourea was obtained as a white solid (m.p. = 120°) and the infrared and mass spectral data together with the elemental analysis confirmed its structure as being the expected N-(o-azidophenyl)-N'-phenylthiourea.



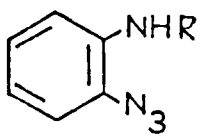
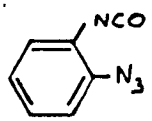
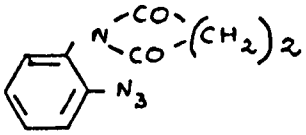
(24)

Thermolytic Decompositions of the o-Azido-Amino Compounds

All the decompositions were carried out in inert solvents, and the products obtained from the various decompositions are shown in Table 1.

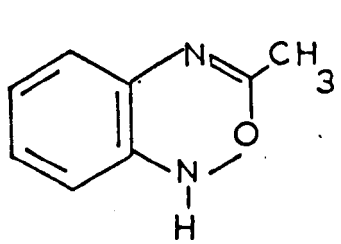
Table 1

Decomposition products of 2-Azidoaniline and its Derivatives

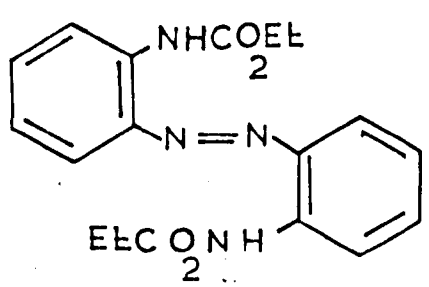
	Solvent	Product	Yield %
H	Chlorobenzene	polymeric materials	-
$COCH_3$	"	N-acetyl-o-phenylenediamine	12
CO Ph	"	N-benzoyl-o-phenylenediamine	9
$-SO_2-C_6H_4 \cdot CH_3(p)$	Bromobenzene	polymeric materials	-
CO_2 Et	Chlorobenzene	azo-compound	75
CONHPh	Bromobenzene	N,N' diphenylurea	10
$CONHC_6H_4 \cdot CH_3(p)$	"	N-phenyl-N'-(p-tolyl)urea	30
$CONH_2$	"	polymeric materials	-
CSNHPh	Chlorobenzene	Benzimidazole-2-thione	29
		aniline	8
	"	benzimidazolone	9
			-
	Bromobenzene	polymeric materials	-

Discussion of Results

Decomposition of o-azidoaniline in chlorobenzene gave only polymeric materials despite a careful thin layer chromatographic investigation of the reaction product. However, with the introduction of acetyl- and benzoyl groups at the nitrogen function, as in the cases of 2-azidobenzanilide (18) and 2-azidoacetanilide, intermolecular processes occurred leading to the formation of N-acetyl-o-phenylenediamine (25) and N-benzoyl-o-phenylenediamine (26), respectively. These were identified by mixed melting point with readily available materials. The lack of products which could possibly arise intramolecularly fits the work reported by Cadogan and his co-workers [147] who showed that oxidative cyclisation of 2-nitrobenzanilide with triethyl phosphite in dry t-butylbenzene gave only 3% of the cyclised product, 3-phenylbenzimidazole. In fact when 2-nitroacetanilide was reduced under similar conditions no benzimidazole was formed, showing that intermolecular reactions are favoured. In fact if intramolecular cyclisation did occur then the oxadiazine (27) could be formed but such a system would probably be thermally unstable. Also it has been shown that aryl nitrenes do not favour the formation of six-membered hetercycles. [85]



(27)



(28)

Polymeric materials were also obtained from the decomposition of o-azido(N-p-tosyl)aniline (19). Thermolysis of ethyl N-(o-azidophenyl)carbamate in chlorobenzene gave the azo compound (28) in surprisingly high yield (75%).

The structure of the azo compound (28) was elucidated on the basis of its physical and analytical evidences. This result was of particular interest in that a literature survey showed that analagous high yields of azo compounds have been obtained only in isolated instances.[148,149] For example, during gas phase pyrolysis of o-(trifluoromethyl)phenyl azide, and during the photolysis of p-methoxy and p-phenylphenyl azide in tetrahydrofuran solution. These reactions afforded the corresponding azo derivatives in 80%, 94% and 81% yield respectively.

Formation of the azo compound (28) in such high yield is as yet unexplained, and current concepts of azo compound formation, as outlined below, do not suggest any reason why this high yield is obtained in this particular reaction. The three main concepts to explain azo compounds are:

1) Dimerisation of the nitrene species.

$$2R\ddot{N}\cdot \rightarrow RN=NR$$

2) Formation of an amino radical leading to aminisation followed by oxidation to the azo compound i.e.

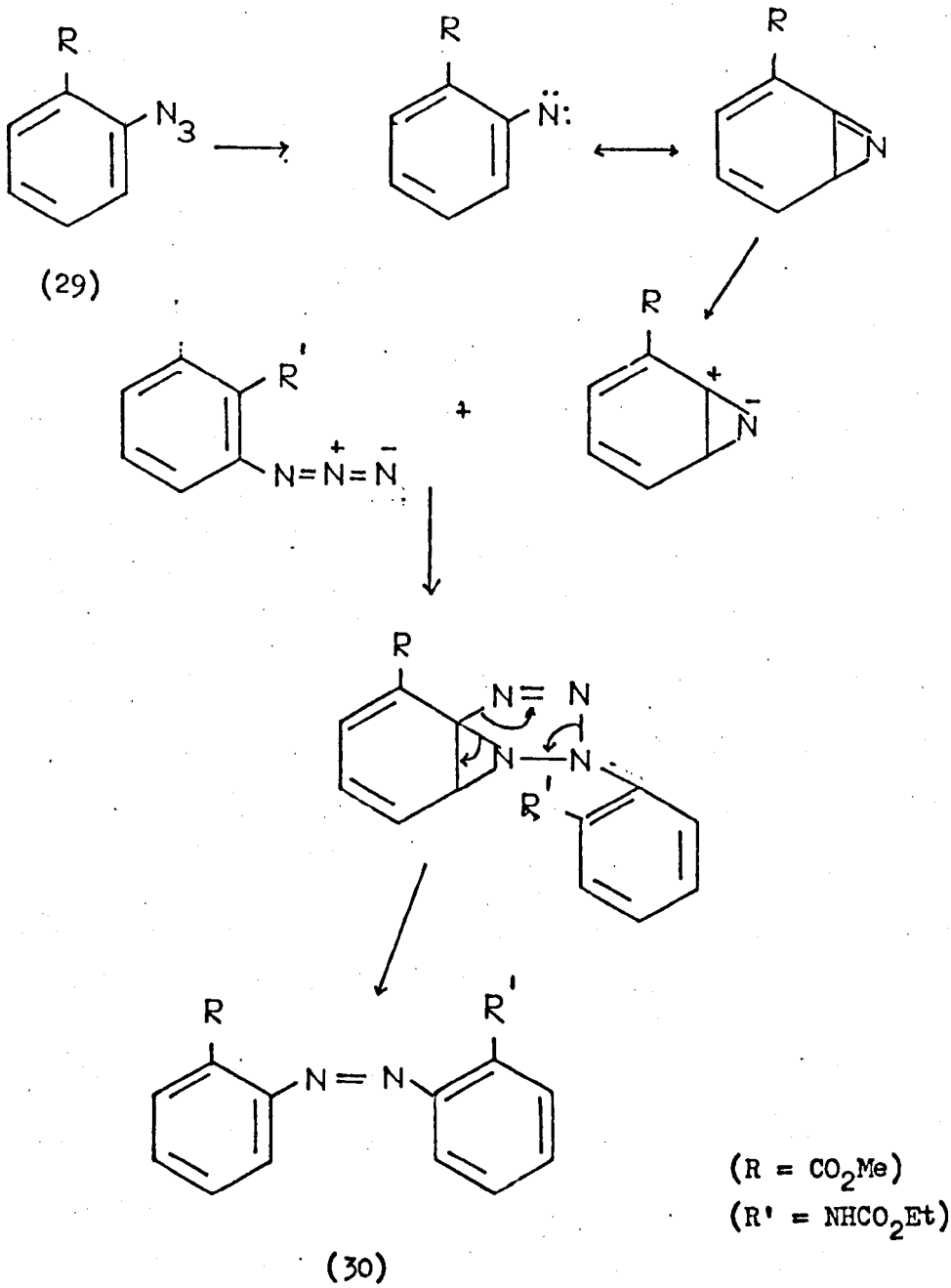
$$R\ddot{N}\cdot \rightarrow R\ddot{N}H \rightarrow RNHNHR \rightarrow RN=NR$$

3) Attack of a nitrene on the azide leading to the azo compound i.e.

$$R\ddot{N}\cdot + RN_3 \rightarrow RN=N-N=N-R \qquad RN=NR + N_2$$

It has been shown by Reiser [150] and his co-workers that two nitrenes can recombine to form azo compounds as the spin is allowed for both the singlet and triplet species. However, this reaction is rarely observed in continuous photolysis of azides because of the low concentration of the free nitrene at any time. However, in flash photolysis where a high nitrene concentration is produced instantaneously, recombination is the preferred path, provided that the solvent is inert. [150] For example, 1-azidonaphthalene in n-hexane gave predominantly 1,1'-azonaphthalene. Possibly the high yield of azo compound from the azidocarbamate is due to a high concentration of nitrene being formed which can either combine to give the azo compound directly or which can attack undecomposed azide as outlined by several workers. [150,151,152] That concentration is important was emphasised when it was shown that reduction of the azide concentration from the usual 10% to 5% in the inert solvent, reduced the yield of the azo compound from 75% to 40%. An alternative theory to explain azo compound formation is that the azo compound could arise by 1,3-dipolar cycloaddition of the unreacted azide to the azirine intermediate in equilibrium with the singlet nitrene. (See Scheme 6).

SCHEME 6



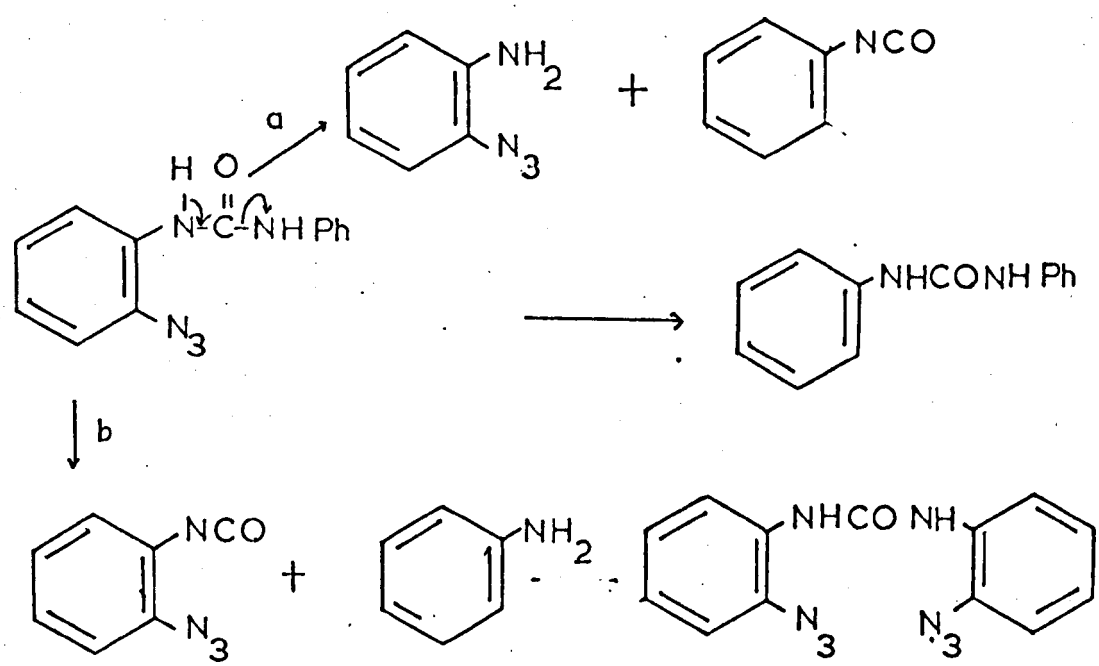
A ready check on this process would be to see whether mixed azo-compound formation is observed on decomposing a mixture of aryl azides. Alternatively, if as proposed by Ogata and his co-workers, photolysis in dichloromethane yields the azirine, then perhaps addition of ethyl-N-(o-azidophenyl)carbamate to the solution would yield a mixed azo compound if the 1,3 dipolar mechanism is operative. Accordingly methyl o-azidobenzoate was photolysed in

dichloromethane for ten hours and to this was then added ethyl N-(o-azidophenyl)carbamate (29) and the mixture stirred in the dark overnight. However the reaction failed in that careful examination of the reaction mixture indicated no mixed azo-compound (30). In fact only polymeric materials and starting azide i.e. azidocarbamate were obtained.

In order to check whether the high yield of azo-compound is general with o-azidocarbamates attempts were made to prepare phenyl N-(o-azidophenyl) carbamate by treating 2-azidoaniline with phenyl chloroformate in pyridine. However, the reaction failed in that, on work up, the product obtained (presumably the required o-azido-carbamate) rapidly underwent hydrolysis and decarboxylation to give o-azidoaniline and phenol. N-(o-Azidophenyl)urea (22) on thermolysis gave only polymeric materials. However, decomposition of N-Phenyl-N'-(o-azidophenyl)urea (20) and N-(o-azidophenyl)-N'-(p-tolyl)urea (21) proved interesting in that products other than tars and triplet based products were obtained.

The azidodiphenyl urea (20) gave as the sole product N,N'-diphenyl urea (31) while the o-azidotolyl urea (21) gave the corresponding product N-phenyl-N'-(p-tolyl)urea (32). These products were confirmed by mixed melting points with available samples. The symmetrical urea may arrive by disproportionation of the unsymmetrical urea, possibly via the isocyanate and amine as indicated in Scheme 7, the diazido-urea decomposing to give tarry products in a similar manner to the N(o-azidophenyl)urea already discussed.

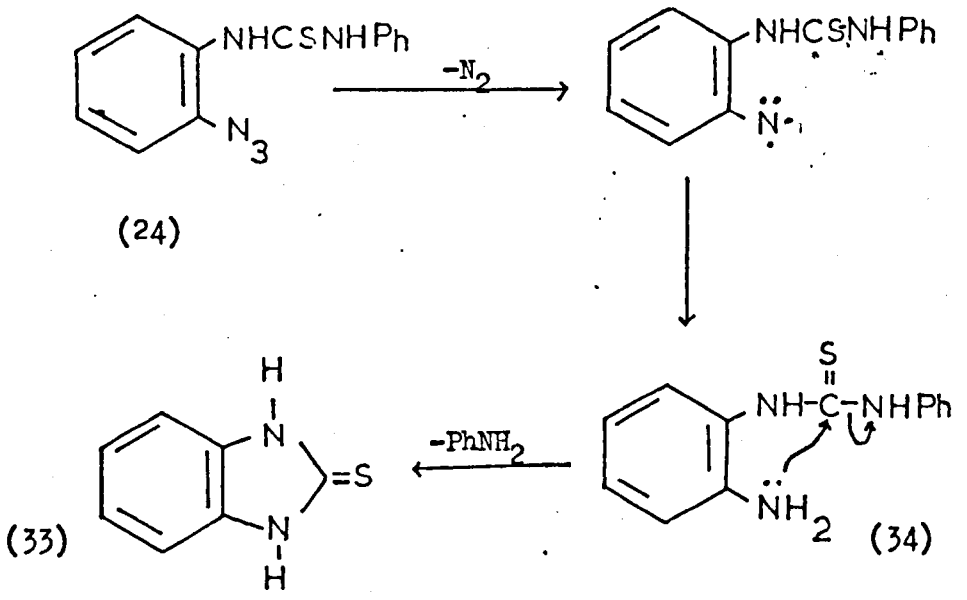
SCHEME 7



Decomposition of the o-azidothiourea (24) in chlorobenzene proved more interesting in that aniline and benzimidazole-2-thione (33), a known compound, were obtained.

Presumably both these products arise by way of a triplet nitrene. Hydrogen abstraction by the diradical nitrene yields the N-(o-aminophenyl)thiourea (34) which under thermal conditions undergoes intramolecular displacement of the aniline residue to yield the benzimidazole-thione as outlined in Scheme 8

SCHEME 8

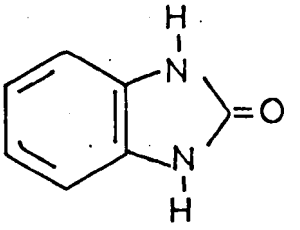


It has been shown that benzimidazole-thiones can be prepared by pyrolysis of aminothioureas.[153,154] The aminothiourea (34) was synthesised by treating o-phenylenediamine with phenyl isothiocyanate in dry benzene, and on thermolysis in chlorobenzene for the same period of time as the azide (24), i.e. 1 hour, it gave a mixture of benzimidazole-2-thione (33) and aniline. As expected the yields of this latter reaction were greater than from the azide decomposition.

An interesting feature of this reaction is the apparently low decomposition temperature of the azide (c.a. 105°), as compared with the temperature of 120-140° for most aryl azides.

Ashby and Suschitzky [155] have noted very low decomposition temperatures for o-azidothiobenzophenone and o-azidothioacetophenone. Possibly with the o-azidothiourea, as in the thioketones, the azide decomposition is being assisted by the neighbouring sulphur containing substituent.

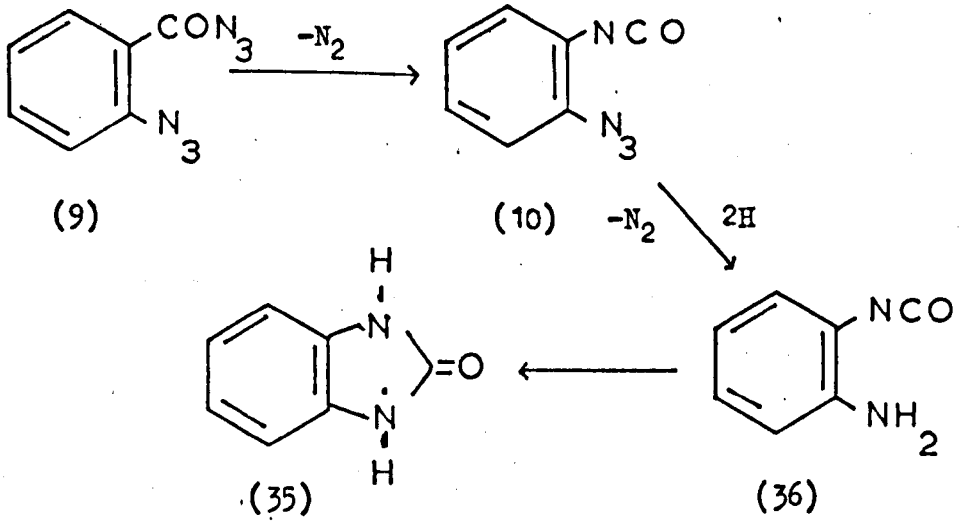
Decomposition of 2-azidobenzoyl azide in dry chlorobenzene gave unexpectedly benzimidazolone (35).



(35)

The benzimidazolone presumably arises by the Curtius rearrangement of the acyl azide to give the o-azidoisocyanate which then undergoes further loss of nitrogen from the aryl azide to give the nitrene, which, as the triplet species, abstracts hydrogen to give the o-aminophenyl isocyanate. Intramolecular addition of the amine to the isocyanate then yields the final product as outlined in Scheme (9).

SCHEME 9



o-Aminobenzoyl azide (8) in boiling acetic anhyride is known to yield the N,N'-diacetyl benzimidazolone [112] and on boiling in dry toluene [89] for three hours benzimidazolone, identical to the azide decomposition product, was obtained in good yield.

g) Photolysis of 2-Azidoanilino Derivatives

Photolysis of several of the o-azidoanilino derivatives, mentioned in the previous section, was carried out in methanol solutions.

Unlike the o-azidocarbonyl compounds already discussed, no azepines were formed and in fact the results in general were disappointing in that in most instances, amines, i.e. triplet nitrene hydrogen abstraction products, and tars were obtained. Alternatively the reaction failed completely, starting materials being recovered.

The azidoureas (20) and (21) were unchanged after prolonged (72 hours) irradiation using a pyrex filter. Irradiation of the azido-carbamate (23) in methanol rapidly produced a dark red-brown solution and once again work up showed predominantly starting materials. This result may in fact be due to the colouration of the solution which shuts out the light. 2-Azidobenzoyl azide in methanol solution undergoes Curtius rearrangement followed by addition of methanol to yield the azidocarbamate, and hence photolysis of this azide was carried out in dry benzene. The photolytic decomposition proved to be the same as for the thermolysis in that benzimidazolone (35) was the sole product.

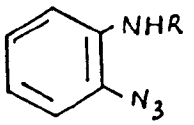
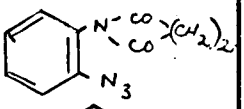
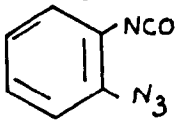
N-(2-azidophenyl)succinimide (15) and 2-azidobenzanilide (18) on photolysis in methanol gave the respective amines, presumably via an intermolecular hydrogen abstraction process by the triplet

nitrene species. The results of photolysis of the o-azidoaniline derivatives are summarised in Table 2.

Summing up, we can conclude that unlike the o-azidocarbonyl compounds, the o-azidoanilino derivatives do not yield azepines when photolysed in methanol solution. Rather, triplet based products are obtained. The actual cause of this difference in behaviour is as yet unexplained, although, as pointed out in Chapter 3, stabilisation of the singlet nitrene by the adjacent carbonyl group is probably a contributing factor.

Table 2

Photolytic Decomposition of o-Azido anilino Derivatives in Methanol

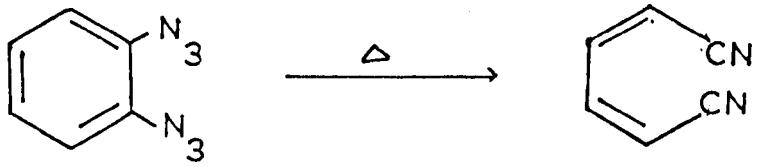
	Solvent	Products	Yield
CO_2 Et	MeOH	starting materials	
CONHPh	"	" "	
CONH-C_6H_4·CH_3(p)	"	" "	
COPh	"	N-acetyl-o-phenylenediamine	17%
H	"	o-phenylenediamine	TRACE
	"	N-(2-aminophenyl)succinimide	30%
	benzene	benzimidozalone	15%

CHAPTER 5

THE SYNTHESIS AND PHOTOLYTIC DECOMPOSITION OF SOME ARYL DIAZIDES

Isolated instances of the decomposition of aromatic diazides [41,42,156,157,158] have been reported. For example, 2-azidophenyl azide (1) on thermolysis in decalin yields CIS-1,4 dicyanobutadiene as outlined in Scheme 1.

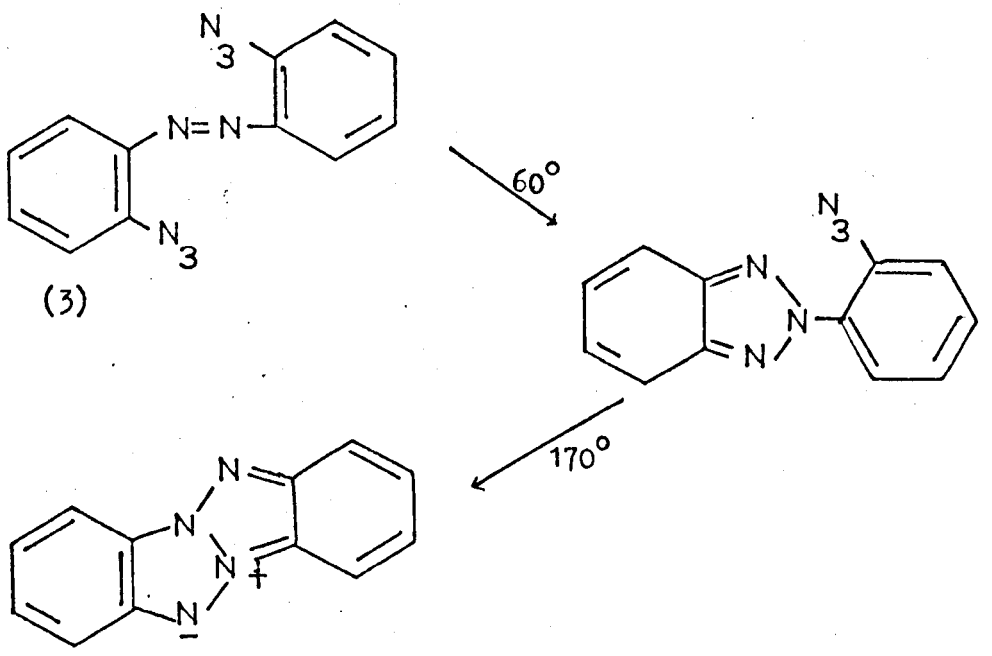
SCHEME 1



(1) (2)

Thermolysis of 2,2'-diazidoazobenzene (3) in decalin gave dibenzo-1,3a,4,6a-tetrazapentalene (4), while thermolysis of diazidobenzylidineazine (5) in 1,2 dichlorobenzene yields 2,2'-bi-indazole (6). Both these latter products are thought to arise by a stepwise decomposition of the azido groups as outlined in Schemes 2 and 3.

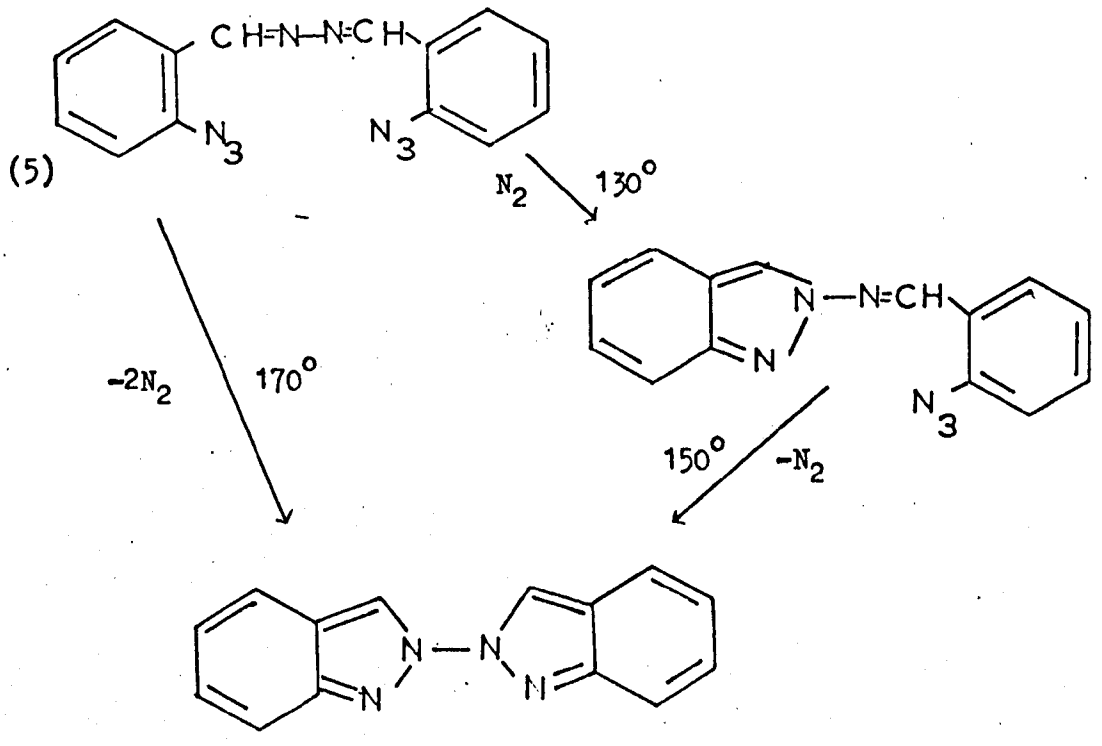
SCHEME 2



(3)

(4)

SCHEME 3

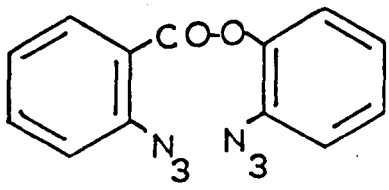


(5)

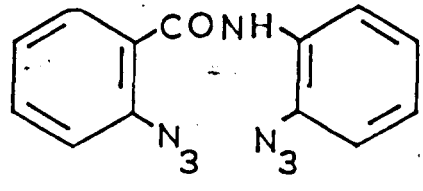
(6)

The first stage in the synthesis of the tetrazapentalene (4) involves assisted loss of nitrogen and proceeds via a concerted mechanism [159] whereas the remaining azide group is believed to yield a nitrene, which cyclises to give the ylide (4).

In chapters 3 and 4 we have shown that azido groups ortho to a carbonyl function in a benzene ring on photolysis in alcohol solution yield 3H-azepines. In contrast, azido groups ortho to amino functions give on decomposition amines and tarry products. In view of this we decided to investigate the photolysis of certain diazides which incorporate both these structural features. The azides, o-azidophenyl 2-azidobenzoate (7) and N-(2-azidobenzoyl)-o-azidoaniline (8) were prepared as outlined below.



(7)



(8)

The principal aim was to determine whether 3H-azepines could be obtained from these diazides, seeing that both had an azido group ortho to the carbonyl function. Thermolysis of these diazides was not considered, since their corresponding monoazides gave tars.

Synthesis of Diazides

The diazidoester (7) was synthesised by the benzoylation of 2-azidophenol with 2-azidobenzoyl chloride under Schotten-Baumann conditions. This azide was obtained as a white solid m.p. = 66° which underwent rapid discolouration on standing in ordinary light. However, its structure was borne out by spectroscopic and analytical data.

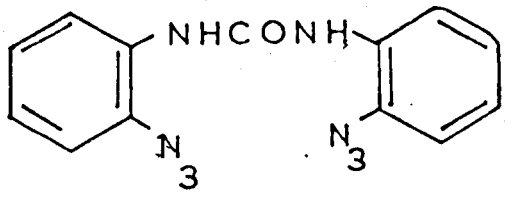
N-(2-azidobenzoyl)-o-azidoaniline (8) was synthesised by benzoylation of o-azidoaniline with o-azidobenzoyl chloride in pyridine. The diazide was obtained as a white solid m.p. = 113°. An infrared spectrum showed ν(NH) at 3290 cm^{-1}, ν(CO) at 1650 cm^{-1} and ν(N_3) at 2160 cm^{-1} features indicative of an azido-amide. The structure was further confirmed by mass spectral and analytical data.

Photolysis of Diazides in Methanol

Like previous photolyses, the decompositions were carried out using a 1% azide solution with the apparatus fitted with a pyrex filter. The azido-ester (7) remained unchanged, after irradiation in methanol solution for seventy-two hours. Since the pyrex filter restricted the wavelength of light (280 n.m.) entering the solution, we thought that a longer wavelength radiation (i.e. the use of quartz filter) would be more effective in bringing about the decomposition of the azide. In fact irradiation of the mixture with a quartz filter for twenty-four hours, brought about the decomposition of the azide but only polymeric materials (in addition to unchanged azide) were isolated. A possible explanation for the poor results may be due to two factors. The first is rapid darkening of the solution which shuts out the incident light, and secondly the light entering the solution may have been so intense that it led to the polymeric materials being formed.

When azido-amide (8) was photolysed in methanol using pyrex and quartz filters respectively, analagous results were obtained. A third diazide N,-N'-di(o-azidophenyl)urea (9) was prepared by reacting o-azidoaniline with o-azidophenyl isocyanate in light petrol.

This diazido-urea was photolysed in methanol solution for seventy-two hours using a pyrex filter, and like previous decompositions only starting materials were obtained.

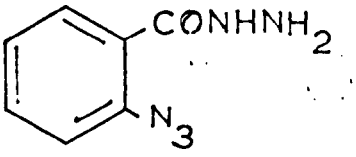


(9)

CHAPTER 6

REACTIONS OF o-AZIDO-ESTERS WITH HYDRAZINES

In chapter 3, the thermolytic and photolytic decompositions of some o-azidocarbonyl compounds was discussed. During this research attempts were made to synthesise o-azidobenzohydrazide (1).

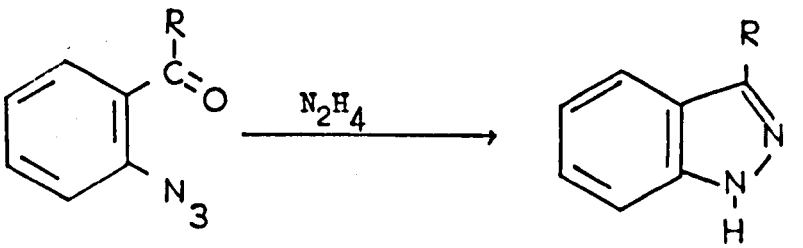


(1)

However, this hydrazide proved difficult to obtain and several intriguing reactions were encountered as are discussed below.

Attempted preparation of the hydrazide by standard procedures i.e. reacting methyl o-azidobenzoate (2) with an excess of hydrazine failed. At room temperature an exothermic reaction took place, with the evolution of nitrogen and ammonia and a pale yellow solid (m.p. = 247°) was obtained. The infrared spectrum of this compound showed absorption at 1630 cm^{-1} indicating the presence of an amidic carbonyl though no NH peak was present and the mass spectrum, showed a molecular ion of 134 units. The product was suspected to be indazoline-3-one (3) and this was confirmed by mixed melting point with an available sample. In the course of this work Professor Rees and his co-workers [160] reported similar reactions on treating o-azidophenyl ketones with hydrazine and obtained indazoles as outlined in Scheme 1.

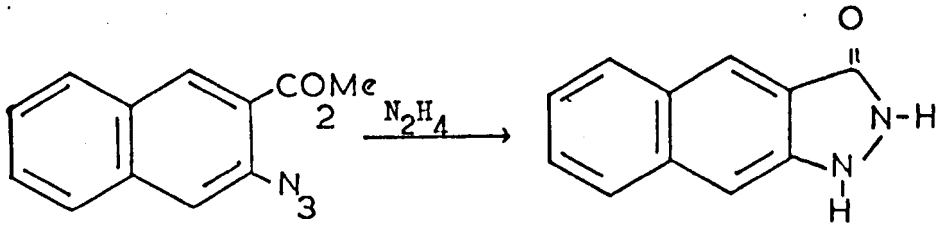
SCHEME 1



(4) (5)

Also more recently Rees and his co-workers [161] have prepared 1,2-dihydrobenz,o[f]indazol-3-one by reacting methyl 3-azido-2-naphthoate (6) with hydrazine in ethanol (Scheme 2).

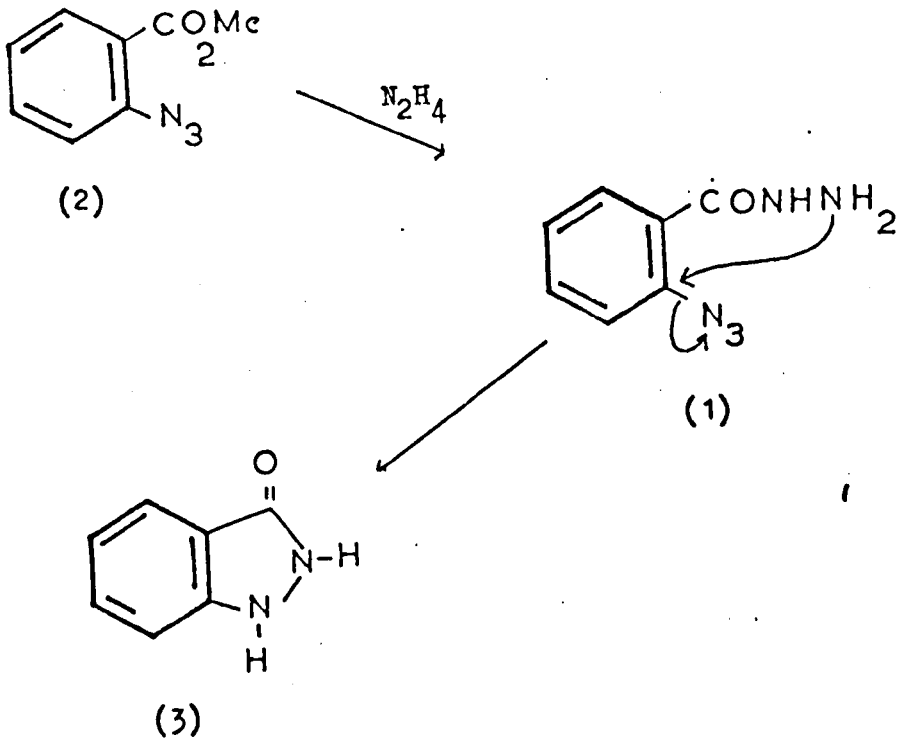
SCHEME 2



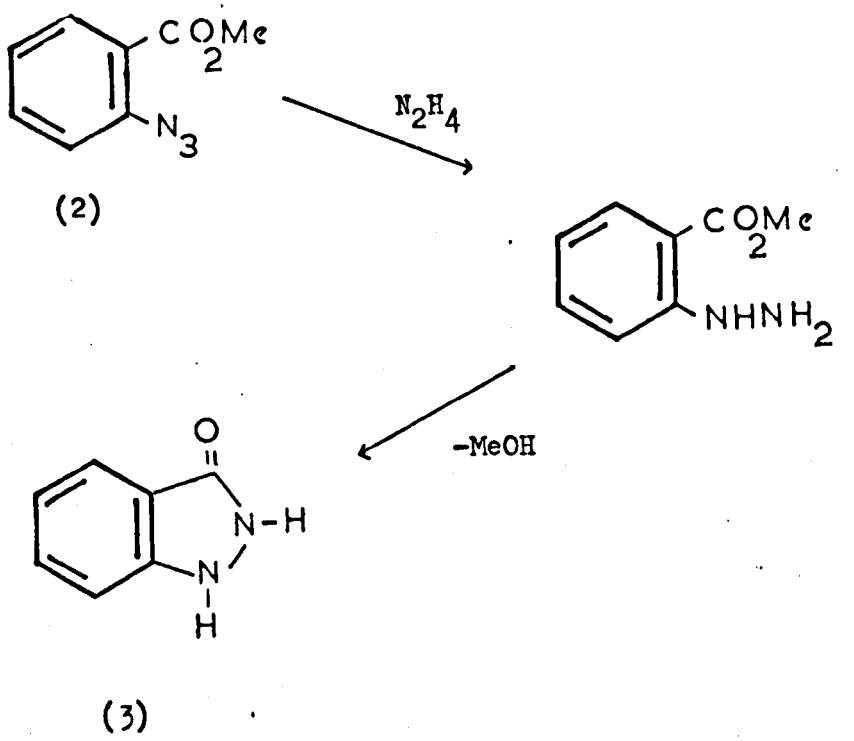
(6) (7)

A factor that was apparent from the discussions of the previous chapters was that a nitrene was not involved since the reaction takes place at temperatures far below those normally associated with aryl azide decomposition. An obvious mode of formation of the indazoline-3-one originally suggested by Rees and his co-workers, [161] involves either nucleophilic displacement of the ester function, followed by the intramolecular displacement of the azido group by the terminal nitrogen of the hydrazide (Scheme 3a) or, alternatively, initial nucleophilic displacement of the azido group (activated by the ortho ester group) by hydrazine followed by nucleophilic displacement of methoxide (Scheme 3b).

SCHEME 3a



SCHEME 3b

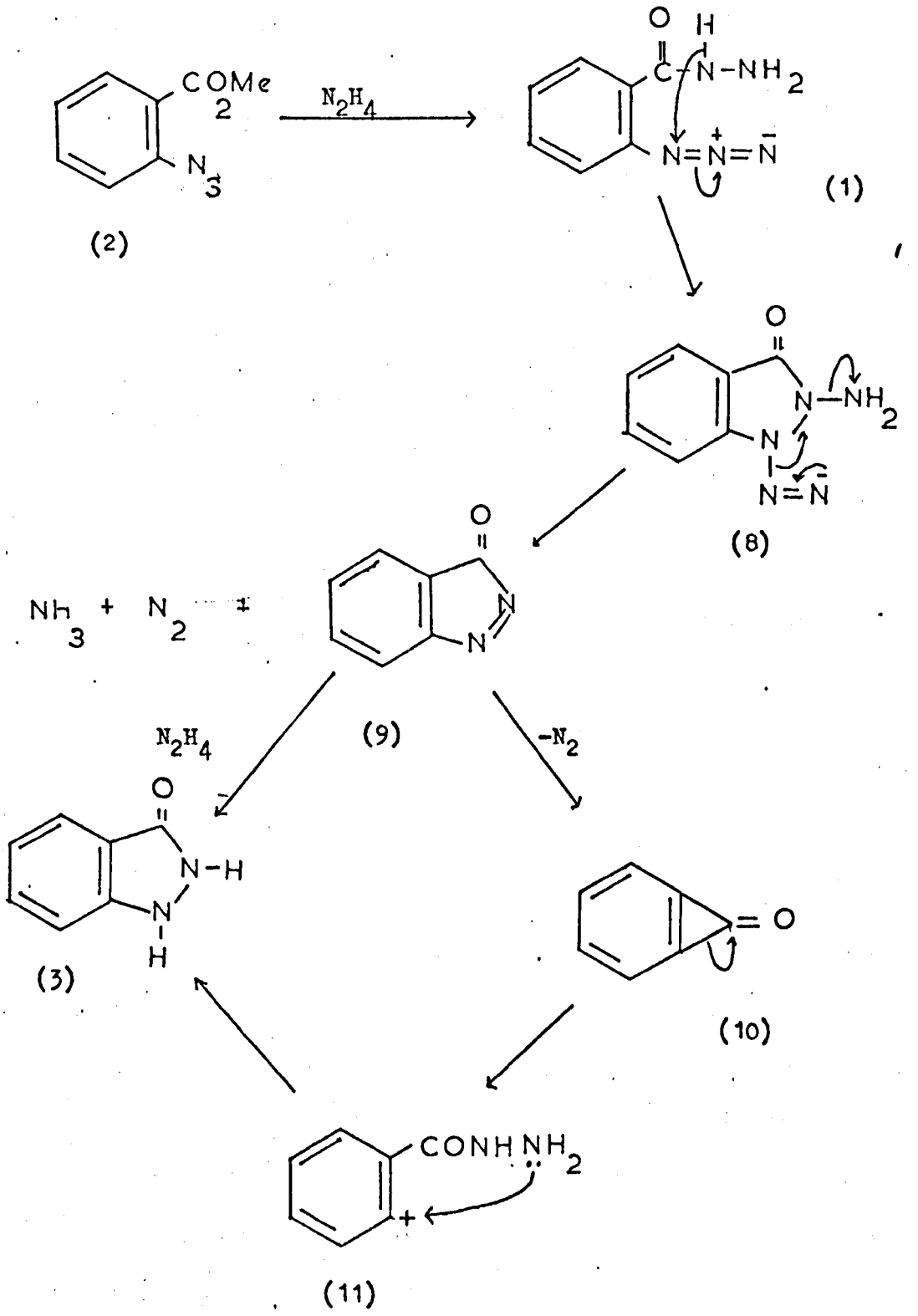


Indazolinone formation by this latter route has been reported[162] with o-chloro-esters in which the halogen is activated by an electron withdrawing (e.g. NO_2) group at the para position. This feature, in which the azido group is displaced from aromatic azides by nucleophiles, is well documented and in every case where it occurs the azido group is activated by substituents with low mobilites.[163,164,165] The activating effect of the (CO_2Me) group as in our example has been shown by Fuller and Miller[166] to be ($\sigma\bar{p}$ 0.819) compared with that of a strong activator (NO_2., $\sigma\bar{p}$ 1.270) and therefore was not considered powerful enough to activate the azido function. The reaction is also unlikely since methyl o-chlorobenzoate reacts normally with hydrazine to give the hydrazide with no loss of chlorine. Experimental evidence against the two proposed mechanisms was obtained by reacting the o-azido-ester with N-methyl hydrazine in ethanol solution. Depending on whether the reaction goes by Scheme 3a or 3b 1-, or 2-methylindazlinone should result. Surprisingly, however, the only product obtained was indazolinone (3) in high yield (70%). It should be noted that the reaction of the azido-ester with N-methylhydrazine was not exothermic and was much slower than with hydrazine and was accomplished only by heating the reactants under reflux in ethanol for several hours.

The reaction was also tried using phenylhydrazine in place of hydrazine and again gave a surprising result in that only starting materials were obtained even after prolonged reflux for ten-hours in ethanol. These reactions illustrate that indazolinone (3) is not formed by a straightforward nucleophilic displacement of the azido group.

Systematic investigation of the reaction conditions showed that an excess of hydrazine is necessary for the reaction to take place and we propose a mechanism for indazolinone formation as outlined in Scheme 4.

SCHEME 4

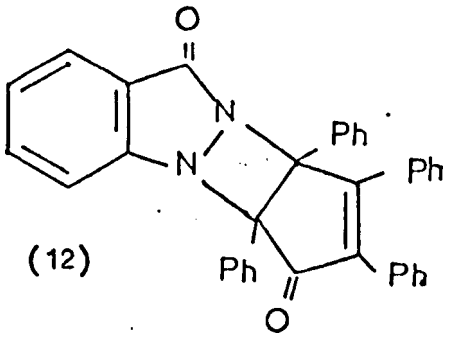


To examine the validity of this mechanism the reactions were investigated more systematically. The possibility of isotopic labelling was considered since, use of labelled hydrazine hydrate should be informative. If the indazolinone contained both labelled species then the latter part of Scheme 4 could be a possibility. If on the other hand the product contained only one labelled species then the product could arise via the 3-indazolone (9). However, isotopically labelled hydrazine could not be obtained. An alternative idea involving labelling the nitrogen of the azide adjacent to the aromatic ring was considered but was not pursued since scrambling can take place in the formation of the azide from the diazonium compound.[167,168]

The o-azidoester and hydrazine when reacted in ethanol in a ratio of 1:1 gave indazoline-3-one in poor yield plus unreacted azide. From this it appeared that the hydrazine was just not forming the hydrazide but was being utilised further in the reaction. However, when the reaction was carried out with the ester-hydrazine ratio of 1:2 the reaction was very slow whereas excess hydrazine produced an exotherimic reaction and indazolinone in high yield. This suggests that the role of hydrazine may be catalytic.

The evolution of gases was also monitored and it was found that two moles of nitrogen was eliminated during the reaction, However, attempts to calculate the amount of ammonia were erratic because indazoline-3-one is slightly acidic and is soluble in ammonia under the aqueous conditions of the reaction. Rees and his co-workers[145] reduced indazoline-3-one with lead tetracetate in dichloromethane and obtained the stable 3-indazolone one of the postulated intermediates in the proposed mechanism. They have shown

the existence of this indazolone (9) by the addition of tetraphenyl cyclopentadienone which traps it as the Diels Alder adduct (12).



(12)

The fact that the intermediate 3-indazolone could be synthesised was helpful in that if this was one of the intermediates of our mechanism, it could be trapped with a suitable diene. The diene used by Rees and his co-workers [145] could not be employed in our reaction because it would react with hydrazine to yield the hydrazone. Furan was then considered as a trapping agent, as a blank experiment showed it had no action on hydrazine.

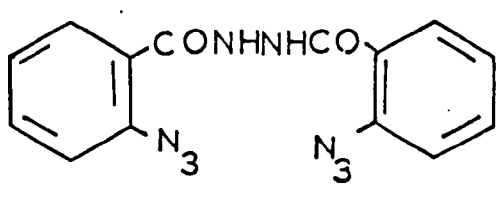
However it failed to trap the indazolone. A possible explanation for this failure may be that the indazolone may be short lived at the reaction temperature.

Also Rees and his workers [145] have shown that this intermediate (9) in the presence of ethanol loses nitrogen to give the benzocyclopropenone (10) which ring opens to produce ethyl benzoate. If this is correct it could explain the evolution of the second mole of nitrogen and supports the latter part of Scheme 4. However, although it is a possibility with hydrazine, it could not explain why 1-, or 2-methyl indazoline-3-one is not formed with N-methylhydrazine. In fact the excess nitrogen could come from

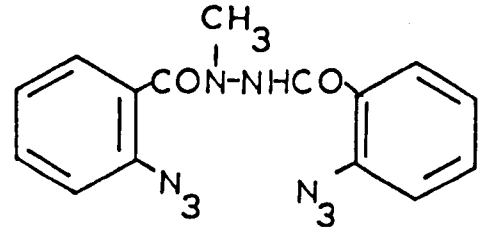
hydrazine itself as Rothenburg [169] has shown that nitrogen is evolved when nitrobenzene is reduced to aniline with hydrazine hydrate in alcoholic solution under reflux. Another possibility for the second mole of nitrogen may arise from the formation of dimide (NH=NH) (13) formed by the action of hydrazine hydrate on the intermediate (9), which then breaks down to produce nitrogen. Similar results have been used to explain the formation of 1,2-dibenzoylhydrazine from the reaction of benzoylhydrazine with diethyl azodicarboxylate, and which results in a vigorous evolution of nitrogen. [170]

There is good evidence that the hydrazide is first formed and this comes from the fact that phenol in addition to indazolinone is formed when phenyl o-azidobenzoate was reacted with hydrazine hydrate in ethanol.

On the basis of the proposed mechanism treatment of o-azidobenzoyl chloride with hydrazine should give the same product i.e. indazoline-3-one. However, when the acid chloride was reacted with excess of hydrazine in either ethanol or pyridine as a solvent surprisingly only the diaryl hydrazine, bis-N,N'-(o-azidobenzoyl) hydrazine (14) was obtained. Similarly the reaction of the acid chloride with N-methylhydrazine gave N-(o-azidobenzoyl)-N'-(o-azidobenzoyl)-N-methylhydrazine (15).

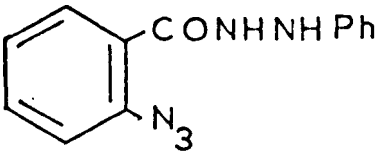


(14)



(15)

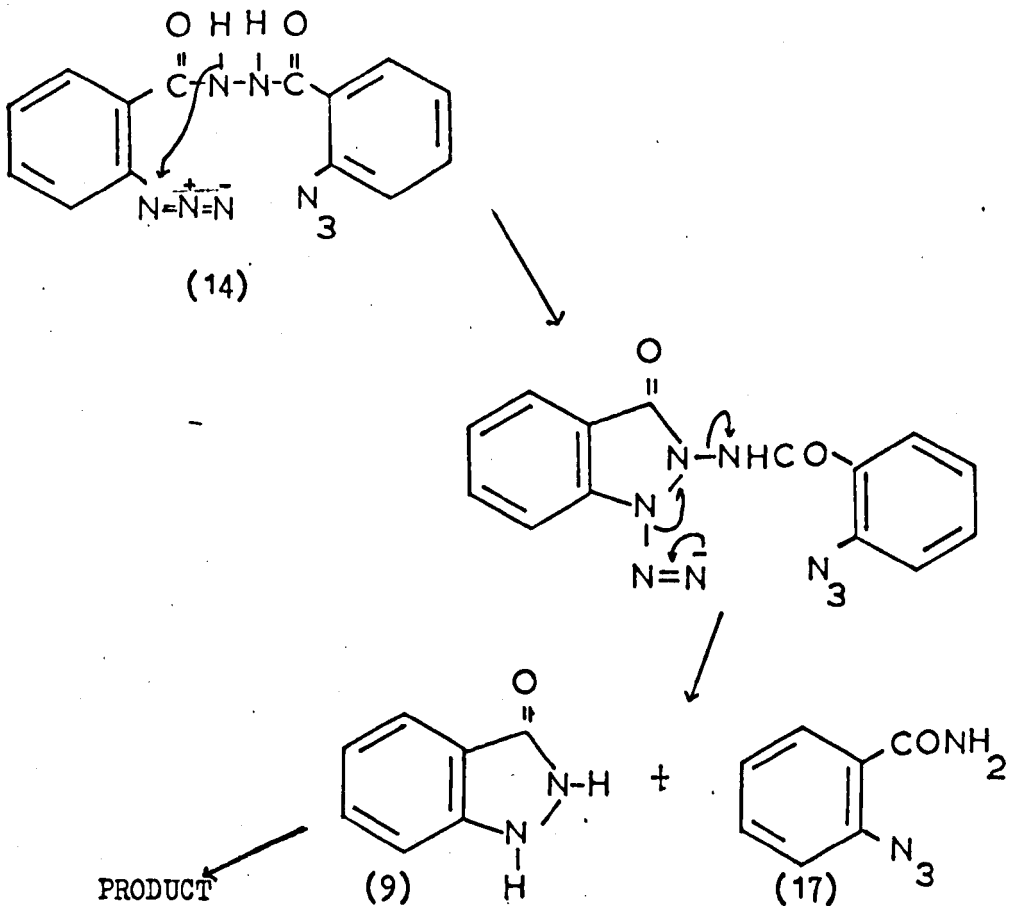
In fact the only case of a mono-hydrazide formation was using phenylhydrazine when N-phenyl-N'-(o-azidobenzoyl)hydrazine (16) was formed in good yield.



(16)

Somewhat surprisingly the diaryl-hydrazine (14) on treatment with excess of hydrazine in ethanol give indazolinone (3) in high yield accompanied by the evolution of ammonia and nitrogen. This reaction is explicable on the basis of the mechanism proposed in (Scheme 4) and would involve the loss of o-azidobenzamide (17) as in Scheme 5.

SCHEME 5

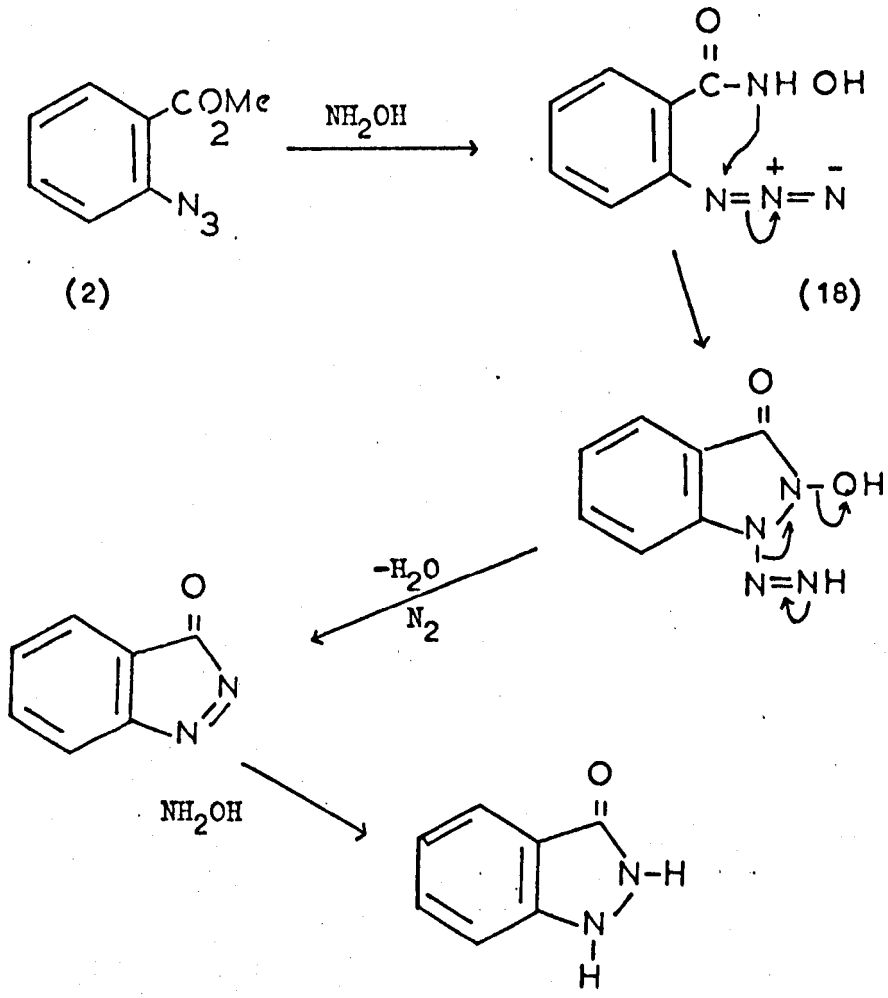


Our failure to isolate the azido-amide as a by product was explained when it was found that the azido-amide itself reacted smoothly with hydrazine hydrate in ethanol to give indazolinone in high yield. The latter reaction is presumably the source of the ammonia in the initial reaction.

o-Azidobenzoic anhydride reacted with hydrazine in ethanol to give indazolinone in poor yield (10%).

As a possible extension to this work, attempts were made to synthesise 2-azidophenyl hydroxamic acid (18) since, if the mechanism given in Scheme 4 is correct, then treatment of the acid (18) should give a similar result, water and nitrogen being lost. The reactions are outlined in Scheme 6.

SCHEME 6



However, attempts to synthesise the azido-hydroxamic acid by the action of hydroxylamine hydrochloride in an aqueous methanolic-sodium methoxide mixture on the azido-ester (1) resulted in the formation of 2-azidobenzoic acid. A possible explanation of this result lies with the rate of hydrolysis of the azido-ester. A qualitative comparison of the rate of hydrolysis of methyl benzoate and methyl o-azidobenzoate was carried out in 5N. sodium hydroxide solution. The former was found to be hydrolysed to the benzoic acid instantaneously whereas in the latter hydrolysis was complete only after twenty-four hours. From these results it was clear that the azido group enhances the rate of ester hydrolysis and consequently hydroxamic acid formation under the conditions employed is not favoured.

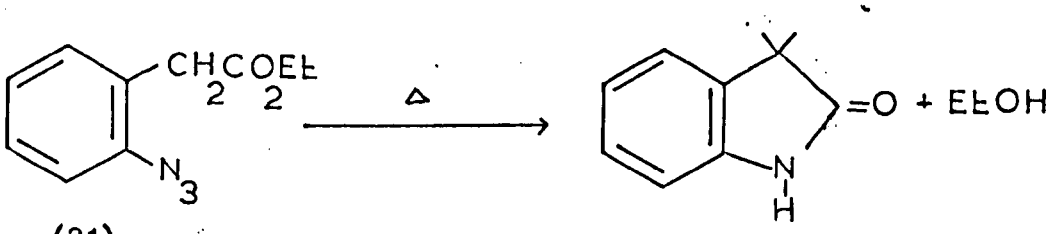
This reaction is obviously intriguing and requires more experimental work before a definate conclusion can be drawn about the mechanism. Unfortunately lack of time prevented further efforts in this direction.

The generality of this reaction is worth investigating since it is the most convenient way of making the indazolinone ring system. Professor Rees [161] has already shown that the reaction is applicable in the naphthalene series and the potential of making indazolinones fused to other ring systems is obvious.

As a preliminary to further investigation we have attempted to extend this reaction to other azide systems. For example the introduction of a CH_2 group between the ester function and the benzene ring (i.e. the ethyl ester of 2-azidophenyl acetic acid (19)) and sulphur systems. The azido-ester (19) was synthesised in

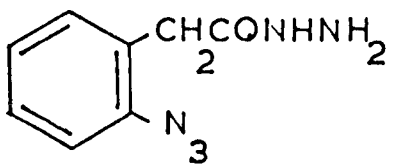
stages. Reduction of ethyl (o-nitrophenyl)acetate (20) led to the amine (21). This was not isolated because an attempt to remove the solvent by gentle heat resulted in oxindole formation as shown by Scheme 7.

SCHEME 7

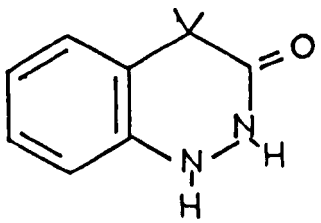


(21)

Consequently the amine was not isolated but was converted directly to its hydrogen chloride salt and then diazotised to give the azido-ester (19). The ester on treatment with hydrazine in ethanol did not however undergo cyclisation to the reduced dinnolone (22) but gave the hydrazide (23).

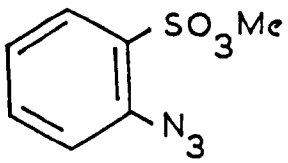


(23)



(22)

The action of hydrazine on o-azidosulphonic acid esters (e.g. 24) should also be interesting.



(24)

However, preliminary attempts to synthesise this hitherto unreported azido-ester have proved abortive. For example, reduction of the methyl o-nitrobenzenesulphonate (prepared by reacting o-nitrobenzene sulphonyl chloride with sodium methoxide) with Palladium charcoal or Raney Nickel and hydrogen gave in each case unidentified high melting metal complexes. Work is continuing on this problem.

EXPERIMENTAL

Part 1

Redistillation of Benzoyl Chloride

This is based on the method of Oakwood and Weisgerber.[87] Commercial benzoyl chloride (100 ml) in benzene (60 ml) was washed with (2 x 100 ml) portions of cold 5% sodium bicarbonate solution. The benzine layer was separated, dried over anhydrous magnesium sulphate and then distilled at 80° to remove benzene and then at 196° to give pure benzoyl chloride which was then stored in a dark bottle under anydrous potassium carbonate. The recovery was 70 ml.

Preparation of Aryl Azides

a) Phenyl Azide

Aniline (20g) in 50% hydrochloric acid (200 ml) in a 500 ml beaker was placed in an ice-bath and the mixture cooled to 0°. To this was then added dropwise a solution of sodium nitrite (14g) in water (50 ml) making certain that after each addition the temperature of the solution did not rise above 5°. This diazonium solution was then added dropwise with constant stirring to a cold mixture containing sodium azide (13g), sodium acetate (100g) in water (200 ml).

The dark yellow oil formed was then extracted with ether (200 ml) and then washed with 4N. sodium hydroxide (50 ml), 10% sodium bicarbonate (2 x 50 ml) and with several washings with water. The etheral layer was then dried over anhydrous magnesium sulphate and the ether carefully removed on a rotary evaporator to a volume suitable for column chromatography. Eluting with dry ether over an alumina column and careful evaporation of the ether on a rotary evaporator gave a pale yellow oil (20.5g) (b.p./2mm/30°) (lit[183] yellow oil).

b) Other Azides

The remaining azides were prepared exactly as phenyl azide i.e. diazotisation of the respective amines (0.2 mol) followed by treatment of the diazonium solution with a mixture of sodium azide (0.2 mol), sodium acetate (100g) in water (200 ml). However in the cases where the azides were liquids i.e. p-toly-; o-methoxy ; and p-chlorophenyl azide removal of the ether after column chromatography gave pure pale yellow liquids. In the other cases, the products were obtained as crystalline solids by reducing the etheral solutions to about 20 ml and the solutions left to stand whereupon crystalline materials were formed which were then filtered. The yields are outlined in Table 1.

Table 1

Preparation of Selected Aromatic Azides

Starting Amines	Product	Yield (gm)	Reference
p-toluidine	p-methylphenyl azide yellow oil	18.6	171 yellow oil
p-anisidine	p-methoxyphenyl azide pale yellow solid m.p. = 35°	14.0	127, 78 (yellow solid) m.p. = 36°
o-anisidine	o-methoxyphenyl azide yellow liquid	15.0	127 (yellow liquid)
p-chloroaniline	p-chlorophenyl azide yellow oil	16.4	172 yellow oil
o-nitroaniline	o-nitrophenyl azide pale yellow solid m.p. = 53°	15.0	173 yellow solid m.p. = 51-53
p-nitroaniline	p-azidophenyl azide straw coloured plates m.p. = 72° C	15.0	174 straw coloured plates m.p. = 71°
o-aminobiphenyl	o-azidobiphenyl yellow prisms m.p. = 49°	18.5	79 yellow prisms m.p. = 48°

Thermolysis of Aryl azides in Benzoyl Chloride

Thermolysis of the prepared azides was carried out in two distinct manners. Method I involved thermolysing all the azides at 150°C in benzoyl chloride until all the azide had disappeared which could be confirmed by infrared spectroscopy, and Method II involved dropping an azide-acid chloride mixture into the hot acid chloride solution at 160° and the mixture was heated under reflux for one hour. This method was applicable to all the azides which are liquids with the exception of o-methoxyphenyl azide.

Decomposition of Phenyl azide in Benzoyl Chloride

Method 1

Phenyl azide (3g) in benzoyl chloride (30 ml) was heated at 145° under nitrogen for 8h. During the decomposition, in addition to nitrogen, hydrogen chloride was given off which was detected by the formation of a white solid on a rod previously dipped in ammonium hydroxide which was suspended into the outcoming gases. The excess acid chloride was distilled off under vacuum and the tarry mass was preabsorbed onto alumina. Eluting with light petroleum (b.p. 40-60°) gave 6-chloro-2-phenylbenzoxazole (0.12g 2%) (m.p. = 98°)(lit.[89] 99°). Further elution with light petroleum (b.p. 40-60°) gave azobenzene (0.09g 2%)(m.p. = 68°). Eluting with benzene gave 2-chlorobenzanilide (0.61g 11%) m.p. = 88° (lit. [184] 88°). Eluting with benzene-ether mixture (1.3) gave a white solid which on crystallisation from ethanol-light petrol (b.p. 40-60°) mixture (50.50) gave benzanilide (2.43g 50%)(m.p. = 162)(lit. [89] 162°). Further elution with ether/methanol mixture (19:1) gave tars.

Method 2

To a hot solution of benzoyl chloride (20 ml) at 160° with constant stirring was added dropwise a solution containing benzoyl chloride (10 ml) and phenyl azide (3g) and the reaction mixture was maintained at that temperature for 1h. The excess solvent was removed by vacuum distillation and the work up was similar to that of Method I. Eluting with light petroleum (b.p. 40-60°) gave azobenzene (0.23g 5%)(m.p. = 68) and with ether gave benzanilide (2.72g 55%) m.p. = 162 (lit. [89] 162°).

Further elution with ether-methanol mixture (19.1) gave polymeric materials.

Unambiguous Synthesis of 6-Chloro-2-phenylbenzoxazole

Method 1

This was accomplished by modification of the general method of benzoxazole synthesis of Suschitzky and co-workers. [90]

p-chlorophenyl azide (1g), benzoic acid (3g) and polyphosphoric acid (20g) was heated at 80° for 1h. and then at 140° for 1 hr. The mixture was then diluted with ice (200g) and then extracted with chloroform (100 ml), washed with 5% sodium bicarbonate (3 x 100 ml) and then dried over anhydrous magnesium sulphate. The chloroform was then removed and the contents preabsorbed onto alumina. Eluting with benzene gave a white solid which, upon recrystallisation from light petroleum (b.p. 40-60°), gave 6-chloro-2-phenylbenzoxazole (0.90g 60%) (m.p. = 98°) (lit. [89] 99°).

Method 2

Alternatively 6-chloro-2-phenylbenzoxazole was synthesised by sublimation of a mixture of equal parts of 2-benzamido-5-chlorophenol and phosphoric pentoxide heated to 230°/15 mm and was crystallised from aqueous acetone as white needles (m.p. = 98-100°).

Unambiguous Synthesis of 5-Chloro-2-phenylbenzoxazole

This method was based on that of Hein and co-workers.[91]

o-Phenoxy-4-chloroaniline (1g) benzoic acid (3g) and polyphosphoric acid (20g) was heated slowly to 250° and the resulting solution was stirred at this temperature for 3h., permitted to cool to 100° and then poured in cold water (400 ml). To this was then added a 50% sodium hydroxide mixture until the slurry was alkaline to phenophthalein indicator paper. The precipitate formed was filtered, washed free of alkali and inorganic salts, dried and recrystallised from aqueous acetone to give white plate of 5-chloro-2-phenylbenzoxazole (0.45g. 30%) (m.p. = 102°).

Decomposition of p-Methylphenyl azide in Benzoyl Chloride

Method 1

The procedure was identical to that of phenyl azide in benzoyl chloride.

Eluting with light petroleum (b.p. 40-60°) gave 4,4'-dimethylazobenzene (0.09g 2%) m.p. = 143° (lit.[89] 141-142°). Elution of the column with benzene-ether (1:1) gave a white solid, which upon recrystallisation from ether, gave N-benzoyl-2-chloro-4-methoxyaniline (1.05g 19%) (m.p. = 138°). Further elution with ether gave a white solid, which upon recrystallisation from ethanol/light petroleum (4.1), gave N-benzoyl-p-toluidine (1.62g 34%)

m.p. = 158 (lit [89] 158°). Eluting with ether-methanol (19:1) gave polymeric materials.

Method 2

This alternate technique and work up was similar to that of phenyl azide. Eluting with light petroleum (b.p. 40-60°) gave 4,4'-dimethylazobenzene (0.19g 4%) (m.p. = 143°). A benzene/ether mixture (1:1) gave N-benzoyl-2-chloro-4-methylaniline (0.66g 12%) m.p. = 138 and elution with ether gave N-benzoyl-p-toluidine (2.14g, 45%) (m.p. = 158) (lit [89] 158°). Finally ether/methanol mixture (19:1) gave tars.

Preparation of t-Butyl Hypochlorite

This compound was prepared to Teiter and Bell method.[175] To a solution containing sodium hydroxide (20g) and water (125 ml) in a three-necked flask was fitted a gas inlet tube which almost touched the bottom of the flask, a gas outlet tube and a mechanical stirrer and the flask was submerged into a water bath at 15°C. To this was then added t-butyl alcohol (18.5g) and water (100 ml) to form an homogeneous solution. With constant stirring chlorine was then passed through the solution at a rapid rate for 30 minutes and then at a slower rate for an additional 30 minutes. The oily upper layer was then separated with the aid of a separating funnel. It was then washed with 50 ml portions of 10% sodium carbonate solution until the washings were no longer acidic to Congo red. It was finally washed three times with equal volumes of water and then dried over anhydrous magnesium sulphate. The yield was 20g (75%).

Unambiguous Synthesis of N-benzoyl-3-chloro-4-methylaniline

2-chloro-4-methylaniline (0.05 mol) was added to pyridine (10 ml) in a 100 ml flask. To this was then added benzoyl chloride (0.05 mol), the flask stoppered and the mixture thoroughly shaken. The contents were poured into water and the solid filtered, washed with 50 ml of 4N.HCl and then with water (2 x 25 ml) and finally dried. Recrystallisation from ethanol gave white needles of N-benzoyl-3-chloro-4-methylaniline (m.p. = 119°). Found : C, 68.45; H, 4.91; N, 5.71; 1, 14.41; $C_{14}H_{12}ClNO$ requires C, 68.45; H, 4.93; N, 5.70, Cl, 14.47), ν max (NH) 3250 cm^{-1}, (CO) 1650 cm^{-1}, mass spectrum m/e 245 (M^+), 210 ($M^+ - 35$).

Unambiguous Synthesis of 4,4'-dimethylazobenzene

This method is based on that of Edwards.[89] Benzoyl peroxide (0.1 mol) in benzene (30 ml) was cooled to 5° in an ice-bath and to this was added p-toluidine (0.1 mol) and the solution stirred for 2h. at room temperature. The solution was then washed with 5% sodium bicarbonate solution and then dried over anhydrous magnesium sulphate. The benzene volume was then reduced and then preabsorbed onto alumina and then chromatographed on alumina. Eluting with benzene gave 4,4'-dimethylazobenzene (m.p. = 141°) (5%).

Unambiguous Synthesis of N-benzoyl-2-chloro-4-methylaniline

a) Preparation of N-chloro-N-benzoyl-p-toluidine

This method is based on that of Mitin and Ulasov.[92] To a conical flask was added p-toluidine (0.05 mol) in methanol (20 ml) followed by 10 ml of a 4% borax solution and the mixture was thoroughly shaken. To this was then added t-butyl hypochlorite (0.1 mol), the flask stoppered, the solution shaken and then left in

the dark for 2h. after which it was poured in water (500 ml). The solid formed was filtered, washed with water and then dried. Recrystallisation from light petroleum (b.p. = 80-100°) gave N-chloro-N-benzoyl-p-toluidine (8.58g 70%) (m.p. = 98°). (Found : C,68.61; H,4.91; N,5.71; 1, 14.45 $C_{14}H_{12}NOCl$ requires C,68.45; H,4.93; N, 5.70; 1, 14.47; ν max 1690 (CO) with (NH) absent mass spectrum m/e 245 (M^+).

b) Rearrangement of N-chloro-N-benzoyl-p-toluidine to N-benzoyl-2-chloro-4-methylaniline

In a 100 ml flask was added methanol (20 mls) and N-chloro-N-benzoyl-p-toluidine (2g) and the contents were refluxed on a water bath for 3 hr. The solution was then cooled and an equal amount of light petroleum (b.p. = 40-60°) was added to it and the solution warmed on a water bath and left to stand whereupon white needles of N-benzoyl-2-chloro-4-methylaniline (m.p. = 138) were formed. The yield was 1.8g (90%) (lit [185] 137°).

Decomposition of 4-methoxyphenyl azide in Benzoyl Chloride

Only Method 1 was employed and like previous work up eluting with light petroleum (b.p. = 40-60°) gave 4,4'-dimethyoxy-azobenzene (0.29g 6%) m.p. = 165 (lit [78] 167°). Eluting with ether gave N-benzoyl-3-chloro-4-methoxyaniline (3.5g (67%)) (m.p. = 169°C) and finally eluting with ether/methanol mixture (19:1) gave polymeric materials.

Unambiguous Synthesis of N-benzoyl-3-chloro-4-methoxyaniline

To a 100 ml flask containing pyridine (20 ml) and 3-chloro-4-methoxyaniline (0.05 mol) was added benzoyl chloride (0.05 mol) and the solution was thoroughly shaken. The mixture was then poured in water (400 ml) and the solid filtered, dried and then recrystallised from ether to give white plates of N-benzoyl-3-chloro-4-methoxyaniline (m.p. = 140). Found : C, 63.82; H, 4.62; N, 5.28; Cl, 13.45 ; $C_{14}H_{12}ClNO$, requires C, 64.06; H, 4.61; N, 5.28; Cl, 13.50), ν max 3250 (NH), 1650 (CO). mass spectrum m/e 261 M^+ , 226 ($M^+ - 35$) and 121($M^+ - 140$).

Unambiguous Synthesis of N-Benzoyl-2-chloro-4-methoxyaniline

To a 100 ml flask containing pyridine (20 ml) and 2-chloro-4-methoxyaniline (0.05 mol) was added benzoyl chloride (0.05 mol) and the mixture was shaken thoroughly for 5 minutes after which it was poured into water. The white solid formed was filtered, washed and then dried.

Recrystallisation from ether/ethanol mixture (3:1) produced white plates (m.p. = 169°). Found : (C, 64.10; H, 4.61; N, 5.27; Cl, 13.48; $C_{14}H_{12}ClNO_2$ requires C, 64.06; H, 4.61; N, 5.28; Cl, 13.50), ν max 3260 (NH), 1655 (CO). Mass spectrum m/e 261 M^+ .

Unambiguous Synthesis of 4,4'-dimethoxyazobenzene

This synthesis was based on the method of Walker and Waters.[78] p-Methoxyphenyl azide (3g) in decaline (30 ml) was heated at 150° for 2 hr. and the excess solvent was removed by vacuum distillation. The residue in benzene was then passed down an alumina column and 4,4'-dimethoxyazobenzene (42%) was obtained as an orange solid (m.p. = 164-165°).

Decomposition of p-Nitrophenyl azide in Benzoyl Chloride

This decomposition was carried out using Method 1 and eluting with ether-methanol mixture (19.1) gave polymeric materials.

Decomposition of o-Nitrophenyl azide in Benzoyl Chloride

Again this decomposition was carried out by Method 1 and eluting the dark mass with benzene on an alumina column gave benzofuroxan (1.84 g 74%) (m.p. = 71°) as a pale yellow solid. Eluting with ether/methanol mixture (19:1) gave a tarry product from which no other products could be characterised.

Unambiguous Synthesis of Benzofuroxan

This method is based on that of Smith and Boyer.[94] To xylene (70 ml) maintained at 100° in a 250 ml round-bottomed flask, equipped with a reflux condenser and a dropping funnel was added o-nitrophenyl azide (3.3g) in xylene (30 ml) and the solution was heated at 100° for 2 hr. The xylene was removed under reduced pressure and the dark oil was stirred with light petroleum (b.p. 40-60°) whereupon the product solidified. It was then filtered, washed with petroleum ether (b.p. 40-60°)(4 x 50 ml) and then crystallised from aqueous ethanol to give benzofuroxan (2.2g, 81%) (m.p. = 70°) as pale yellow prisms (lit[95] 71°).

Decomposition of p-Chlorophenyl azide in Benzoyl Chloride

Decomposition was carried out by Method 1 and eluting with benzene gave 4,4'-dichloroazobenzene (0.44g, 9%) (m.p. = 188°) (lit[89] 187°). Eluting with ether gave p-chlorobenzanilide (1.18g, 24%) (m.p. = 192°) (lit[89] 192°) and finally with ether-methanol mixture (19.1) gave tars.

Decomposition was also carried out by Method 2 and eluting with benzene gave 4,4'-dichloroazobenzene (0.7g 15%) m.p. = 188° and with ether 4-chlorobenzanilide (0.7g (15%)) m.p. = 191° and finally with ether-methanol mixture (19:1) gave polymeric material.

Unambiguous Synthesis of 4-Chlorobenzanilide

To a 5% sodium hydroxide solution (30 ml) in a 100 ml flask was added p-chloroaniline (0.01 mol) and benzoyl chloride (0.01 mol), the flask stoppered and the mixture shaken for 5 minutes. The white solid formed was filtered, washed with water and then dried. Recrystallisation from aqueous ethanol gave white plates of 4-chlorobenzanilide (75%) (m.p. = 192°)(lit[89] m.p. = 191°)

Decomposition of 2-Azidobiphenyl in Benzoyl Chloride

Decomposition was only carried out by Method 1 and eluting with light petroleum (b.p. 60-80) gave N-benzoylcarbazole (10%) as a white crystalline solid (m.p. = 98°) (lit [187] m.p. = 98°). Eluting with benzene gave carbazole (75%) m.p. = 238° (lit [79] m.p. = 237-238°).

Preparation of N-Benzoylcarbazole

To benzoyl chloride (30 ml) was added carbazole (0.05 mol 8.35g) and the mixture heated under reflux for 6 hr. The benzoyl chloride was removed under vacuum and brown mass was then titurated with benzene. Recrystalisation from ether gave N-benzoylcarbazole (83%) (m.p. = 68°) (lit [186] m.p. = 68°).

Preparation of N-Chlorobenzanilide

Method 1

This is based on the method of Orton and Chattaway.[97] In a 500 ml flask containing potassium bicarbonate (50g) in water (200 ml)

was added bleaching powder (0.2 mol) and benzanilide (0.1 mol) and the mixture stirred for 1 hr. The mixture was then extracted chloroform (2 x 200 ml) and then dried over anhydrous magnesium sulphate. Removal of the chloroform produced unreacted benzanilide (19.6g).

Method 2

This was based on the method of Mitin and Vlasov.[92] To a 100 ml flask was added, benzanilide (0.05 mol, methanol (20 ml) and 10 ml of a 4% borax solution and the mixture was thoroughly shaken. To this was then added t-butyl hypochlorite (0.1 mol), the flask stoppered, shaken, and then left in the dark for 2 hrs. after which it was poured in water (500 ml). The white solid formed was filtered, washed with water (2 x 100 ml) and then dried. Recrystallisation from light petrol (b.p. 40-60°)/ethanol mixture (3.1) gave white plates (m.p. = 78°) (lit [97] m.p. = 77°). The yield was 8.5g (85%).

Decomposition of N-Chlorobenzanilide in Benzoyl Chloride

a) Benzoyl Chloride (pure)

N-chlorobenzanilide (1g) in benzoyl chloride (10 ml) was heated under reflux for 4 hr. The solvent was removed under reduced pressure and the solid was eluted with ether on alumina to give p-chlorobenzanilide (m.p. = 192°) (lit [89] 191°).

b) Benzoyl Chloride (saturated with HCl gas)

The procedure was identical to method (a) and gave p-chlorobenzanilide (0.94g) (m.p. = 192°).

Decomposition of o-methoxyphenyl Azide in Benzoyl Chloride

Decomposition was carried out by Method 1 and the work up similar to previous decompositions. Eluting with ether gave N-benzoyl-2-chloro-6-methoxyaniline (2.89g 55%) m.p. = 135° (lit [176] 136°) and with ether-methanol mixture (19.1) gave tars.

Unambiguous Synthesis of N-Benzoyl-3-chloro-6-methoxyaniline

To an 100 ml flask containing pyridine (20 ml) and 2-amino-4-chloroanisole (0.05 mol) was added benzoyl chloride (0.05 mol) and the mixture shaken and then poured into water. The solid was then filtered, washed with water, dried and then recrystallised from aqueous ethanol to give N-benzoyl-3-chloro-6-methoxyaniline (75%) (m.p. = 77°).

Unambiguous Synthesis of N-Benzoyl-2-chloro-6-methoxyaniline

The benzoylation of 2-amino-3-chloroanisole was carried out using the same molar quantities and the same conditions as the previous experiment and recrystallisation from aqueous ethanol gave N-benzoyl-2-chloro-6-methoxyaniline (84%) (m.p. = 135) (lit [176] 135°).

Decomposition of 2-Azidobiphenyl in Acetic Anhydride

This procedure was identical to that of Method 1 for the benzoyl chloride decomposition but acetic anhydride was employed as the solvent. The work up was also identical and eluting with benzene gave N-acetylcarbazole (3%) m.p. = 68 (lit [186] 68°) and with ether gave carbazole (72%) m.p. = 237° (lit [79] 237-238°).

Decomposition of Phenyl Azide in Benzoyl Chloride under Molecular Oxygen

This decomposition was carried out by Method 1 but the thermolysis was carried out under molecular oxygen instead of nitrogen. The work up was again similar to previous decompositions and eluting with benzene gave o-chlorobenzanilide (12%) m.p. = 88 (lit [184] 88°) and with ether gave benzanilide (20%) (m.p. = 162°).

Photolysis of Aryl Azides in Benzoyl Chloride

a) Phenyl Azide in Benzoyl Chloride

A solution of phenyl azide (1g) in benzoyl chloride (100 ml) was photolysed with a 125W medium pressure lamp (with pyrex filter) for 48h. The benzoyl chloride was removed under reduced pressure and the oily residue was preabsorbed onto alumina and eluting with light petroleum (b.p. 40-60°) gave 0.95 g of unreacted phenyl azide. However, when a quartz filter was employed irradiation was carried out for 24h. and the tarry mass worked up as above and eluting with ether-methanol mixture (19:1) gave polymeric materials.

b) p-Methylphenyl Azide in Benzoyl Chloride

This decomposition was similar to that of phenyl azide. Irradiation (using a pyrex filter) gave unreactive azide whereas (with a quartz filter) gave tars.

c) p-Methoxyphenyl Azide in Benzoyl Chloride

Irradiation (with a pyrex filter) gave unreactive starting materials. However irradiation with a quartz filter for 24 hr. and eluting the alumina column with light petroleum (b.p. 40-60°) gave 4,4'-dimethoxyazobenzene (0.03g 2%) (m.p. = 164) and with ether gave

N-benzoyl-2-chloro-4-methoxyaniline (0.35g 20%) (m.p. = 169°). Eluting with ether-methanol (19:1) gave tars.

d) p-Chlorophenyl Azide in Benzoyl Chloride

This decomposition was again similar to that of phenyl azide. Irradiating the 1% azide solution (with pyrex filter) for 48 hr. followed by removal of the solvent under reduced pressure gave unchanged starting material. However irradiation with quartz filter for 24h. gave polymeric materials.

Preparation of Benzoyl Azide

To an aqueous solution (50 ml) of sodium azide (0.02 mol) containing one drop of pyridine, benzoyl chloride (0.02 mol) was added with shaking, and a colourless oil separated which solidified on cooling. The solid was recrystallised from light petroleum (b.p. = 40-60°) to yield benzoyl azide (2.5g, 85%) (m.p. = 33°) (lit [112] m.p. = 32).

Decomposition of Benzoyl Azide in Benzoyl Chloride

A solution of benzoyl azide (3g) in acetic anhydride (10 ml) was added dropwise to boiling acetic anhydride (20 ml). The solution was then heated under reflux for 1 hr. The mixture was then carefully distilled at 62-63° to give phenyl isocyanate (1.58g 65%).

The Decomposition of p-Methoxyphenyl azide in Anisole and Benzoyl Chloride

p-Methoxyphenyl azide (2g) in benzoyl chloride (15 ml) and anisole (15 ml) were heated under reflux for 2h. at 140°. On cooling extracts from the mixture was fed into a high pressure gas-liquid chromatogram and the peaks obtained did not correspond to any chlorinated anisoles. (This fact was substantiated by passing through a mixture of o-, m-, and p-chloroanisole through the chromatogram and comparing these peaks with those of the reaction mixture.

Part 2

Preparation of o-Azido-Carbonyl Compounds

Preparation of N-(2-azidobenzoyl)aniline

In a 100 ml flask was added aniline (6g) and aqueous 10% sodium hydroxide (25 ml) and to this was then added impure 2-azidobenzoyl chloride (5g), the flask stoppered and the mixture shaken for 5 minutes. The crude benzoyl derivative which appeared as a green oil was then poured in water (200 ml) where it solidified. The product was washed with water and dried. The product was then dissolved in hot ethanol and to it was added 1g of decolourising charcoal and the mixture heated and then filtered. On cooling a pale white crystalline solid of N-(2-azidobenzoyl)aniline (6.1g 93%) (m.p. = 134°) ν_{max} 3300 (NH), 2130 (N_3), 1665 (C=O). (Found : C, 65.43; H, 4.22; N, 23.45; $C_{13}H_{10}N_4O$ requires C, 65.54; H, 4.23; N, 23.52). Mass spectrum m/e 238 (M^+).

Preparation of 2-Azidobenzamide

In a 100 ml beaker submerged in ice was added concentrated ammonia solution (15 ml S.G. = 0.88) and to this was added dropwise (carefully) impure 2-azidobenzoyl chloride (5g). The pale brown solid formed was filtered, washed with 2 N. HCl (30 ml) and then with water (2 x 50 ml) and finally dried. Recrystallisation from aqueous ethanol gave 2-azidobenzamide (4.4g 97%) (m.p. = 136°) as white needles (lit [16] 135°).

Preparation of N-(2-Azidobenzoyl)-o-anisidine

This azide was prepared by a method similar to that of N-(2-azidobenzoyl)aniline and this was accomplished by adding o-anisidine (3.6g) in 10% NaOH solution (20 ml) to 2-azidobenzoyl

chloride (5.4g). The solid formed was washed with water (2 x 50 ml), dried and then recrystallised from ethanol to give N-(2-azidobenzoyl)-o-anisidine as white plates m.p. = 98° (6.77g 90%); ν_{max} 3380 (NH), 2130 (N_3), 1670 (CO); mass spectrum m/e 253 (M^+). (Found : C, 66.07; H, 5.19; N, 22.19; $C_{14}H_{12}N_4O$ requires C, 66.0; H, 5.17; N, 22.12).

Preparation of Methyl o-Azidobenzate

This azide was prepared by the general method of Smith and Brown.[79] Methyl Anthranilate (0.1 mol) was diazotised in the usual manner and the diazonium solution was added to a mixture containing sodium azide (0.1 mol) and sodium acetate (60g) in water (200 ml). The dark oil formed was extracted with ether (200 ml) washed with 5% sodium hydroxide (2 x 25 ml) and with water (2 x 50 ml). The etheral extract was then dried over anhydrious magnesium sulphate and then columned over alumina with dry light petroleum (b.p. 40-60°) and careful evaporation of the petroleum ether gave methyl o-azidobenzoate (14.2g 80%) as a pale yellow oil (lit[127] yellow oil).

Preparation of 2-Azidobenzoyl Chloride

In 500 ml flask fitted with a reflux condenser, the top of which had a drying tube, was added dry benzene (200 ml) o-azidobenzoic acid (9.6g) and thionyl chloride (10 ml) and the mixture was heated gently to initiate the reaction. The solution was then thoroughly stirred (with a magnetic stirrer) and when the reaction was complete a clear solution was formed. The excess thionyl chloride was removed by careful distillation using a water pump leaving o-azidobenzoyl chloride as a dark yellow oil (9.1g 85%) ν_{max} 1800 and 1750 (CO), 2145 (N_3).

Preparation of Phenyl o-Azidobenzoate

To an impure solution of o-azidobenzoyl chloride (3.g) in pyridine (10 ml) in a 100 ml flask was added phenol (6.g). The flask was stoppered and the mixture thoroughly shaken after which it was poured in 200 ml of dilute HCl solution. The mixture was then transferred to a separating funnel and the contents extracted with ether (200 ml). The ether layer was separated, washed with 5% NaOH (3 x 25 ml), and several washings with water. Finally it was dried over anhydrous magnesium sulphate and the ether volume carefully reduced on a rotary evaporator. It was then columned on alumina with ether to give phenyl o-azidobenzoate (3.8g 96%). A pure sample (m.p. = 50°) was obtained as white plates upon re-crystallisation from light petroleum (b.p. 60-80°) ν_{max} 1740 (CO); 2150 (N_3), (Found : C, 67.22; H, 3.78; N, 17.50; $C_{13}H_9N_3O_2$ requires C, 67.19; H, 3.79; N, 17.56), mass spectrum m/e 239 (M^+).

Preparation of 2-Azidobenzoic Anhydride

The preparation was based on the method of Smalley and Suschitzky.[129] o-Azidobenzoic acid (5g) in 250 ml flask was carefully neutralized (Phenolphthalin) with 2N sodium hydroxide solution. To this was then added 2 drops of pyridine and then benzoyl chloride (4.2g). The flask was then stoppered and the mixture shaken, whereupon an oily layer was formed at the bottom of the flask. This was then extracted with ether (100 ml), washed with dilute HCl (20 ml), 5% NaOH (50 ml) and finally with water (2 x 50 ml). The etheral solution was then dried over anhydrous $MgSO_4$ and careful removal of the ether on a rotary evaporator gave 2-azidobenzoic anhydride as a pale yellow oil. ν_{max} 1820 and 1755

(CO), 2145 (N_3); (Found : C, 62.81; H, 3.37; N, 15.70; $C_{14}H_9N_3O_3$ requires C, 62.92; H, 3.39; N, 15.72). Mass spectrum m/e 267 (M^+).

Preparation of o-Azidobenzoic Acid

This was synthesised by the method of Rao and Venkataraman.[122] Anthranilic acid (0.1 mol) was diazotised in the usual manner using sodium nitrite (0.1 mol) in 50% HCl solution. The diazonium solution was then added to a solution containing sodium azide (0.1 mol) and sodium acetate (70g) in water (200 ml). The resulting yellow solution was then acidified with 2N.HCl to give a white solid which was filtered, washed with water (2 x 200 ml) and then dried. Recrystallisation from benzene gave o-azidobenzoic acid (13g, 80%) (m.p. = 144°) (lit [121,122] 142-144°).

Preparation 2-Azidophenylthioester.

To thiophenol (2g) in an 100 ml flask containing 10% NaOH solution (20 ml) was added 2-azidobenzoyl chloride (1.8g). The flask was stoppered and the mixture shaken. A dark yellow solid was formed, which was filtered, washed with water (2 x 50 ml) and then dried. The solid was then columned on alumina with ether to give 2-azidophenylthioester (2.9g 93%). A white crystalline solid (m.p. = 78°C) was obtained by recrystallisation from light petroleum (b.p. 40-60°). ν_{max} 1685 (C(=O)-S), 2110 (N_3); (Found : C, 60.81; H, 3.62; N, 16.70 $C_{13}H_9N_3OS$ requires C, 61.06, H, 3.60; N = 16.50; Mass spectrum m/e 255, (M^+).

Preparation of Methyl o-azido-4-chlorobenzoate

Preparation of Methyl 2-amino-4-chlorobenzoate

Methyl 2-nitro-4-chlorobenzoate (8g) in methanol (100 ml) was reduced with 1g of 10% palladium charcoal catalyst in the presence of hydrogen under atmospheric conditions until the hydrogen uptake ceased. The catalyst was then removed by filtration and evaporation of the solvent gave methyl o-amino-4-chlorobenzoate m.p. = 68° (lit [177] 69°).

Preparation of Methyl 2-azido-4-chlorobenzoate

In a 200 ml flask was added methyl o-amino-4-chlorobenzoate (10g) and 50% HCl (50 mls) and the solution cooled to 0°C in an ice-bath. This solution was then diazotised in the usual manner with sodium nitrite (3g) in water (15 ml) and the diazonium solution was then added to a mixture containing sodium azide (2.9g) and sodium acetate (30g) in water (20 ml). The oily layer formed was extracted with ether (200 ml), washed with 5% NaOH solution (50 ml) and finally with water. The ether solution was then dried over anhydrous magnesium sulphate. Evaporation of the ether left a dark yellow oil which was then columned over alumina with light petroleum (b.p. - 40-60°) to give methyl o-azido-4-chlorobenzoate (10.1g) as a pale yellow oil. ν_{max} 1730 (C=O); 2130 (N_3), (Found : C, 45.60; H, 2.87; N, 19.82; Cl, 16.71, $C_8H_6N_3O_2Cl$ requires C, 45.41; H, 2.86; N, 19.86, Cl, 16.75). Mass spectrum m/e 211 (M^+).

Preparation of Methyl 4-azidobenzoate

Methyl-4-nitrobenzoate

4-Nitrobenzoic acid (0.1 mol) in methanol (200 ml) and concentrated sulphuric acid (2 ml) in a 500 ml flask fitted with a

reflux condensor was refluxed for 48 hr. The excess methanol was removed on a rotary evaporator to give methyl-4-nitrobenzoate (83%). This was sufficiently pure for the next stage.

Methyl 4-aminobenzoate

Methyl 4-nitrobenzoate (15g) in methanol (200 ml) was reduced with 10g of Raney-Nickel under hydrogen (50 Atmospheres) for 12h. The catalyst was removed by filtration and evaporation of the methanol gave methy 4-aminobenzoate (12g, 96%) (m.p. = 110°) as a white solid (lit [180] 112°).

Methyl 4-azidobenzoate

Methyl 4-aminobenzoate (10g) was added to a solution containing conc. HCl (40 ml) and water (250 ml) in a 500 ml beaker. The solution was then cooled to 0°C and the mixture diazotised in the usual manner by adding sodium nitrite (5g) in water (20 ml). The diazonium solution was then added to a solution containing sodium azide (4.7g) and sodium acetate (50g) in water (100 ml). The white solid formed was extracted with ether (100 ml) and washed with the usual reagents and then dried. Revoval of the ether followed by recrystallisation from light petroleum (b.p. 40-60) gave methyl 4-azidobenzoate (80%) m.p. = 39° (lit [127] 39-40°).

Preparation of 2-Chloro-5-azidobenzamide

5-Nitro-2-chlorobenzoic acid

In a litre beaker, suspended in an ice bath, was added fuming nitric acid (200 ml) and to this was then added 2-chlorobenzoic acid (20g) in small portions over 15 minutes making certain that the

temperature did not rise over 30° after each addition. The mixture was then stirred for 1 hr. after which it was poured in 500g of ice. A white solid of 5-nitro-2-chlorobenzoic acid was formed which was washed with water (4 x 100 ml) and then dried (m.p. = 164). The yield was 24g (92%) (lit [181] 165°).

5-Amino-2-chlorobenzoic Acid

5-Nitro-2-chlorobenzoic acid (20g) in methanol (200 ml) was reduced with Raney-Nickel under hydrogen in the Baskerville (50 ATMS) for 14h. The catalyst was removed by filtration and evaporation of the solvent gave 5-amino-2-chlorobenzoic acid (94%) (m.p. = 183°) (lit [181] 185°).

5-Azido-2-chlorobenzoic Acid

5-Amino-2-chlorobenzoic acid (10g) was diazotised in the usual manner using $NaNO_2$ (0.1 mol) in excess of hydrochloric acid at 0°C. The diazonium solution was then added to a mixture of sodium azide (3.9g) and sodium acetate (50g) in water (100 ml). The resulting solution was acidified with 4N.HCl and the white solid formed was filtered, washed with water (3 x 100 ml), dried, and then recrystallised from benzene to give white plates of 5-azido-2-chlorobenzoic acid (10.1g, 94%) (m.p. = 141°). ν_{max} 1720 (CO), 2130 (N_3). (Found : C, 42.45; H, 2.04; N, 21.31; Cl 17.98; $C_7H_4N_3O_2Cl$ requires C, 42.55; H, 2.04; N, 21.27; Cl, 17.94). Mass spectrum m/e 197 (M^+), 162, ($M^+ - 35$).

5-Azido-2-chlorobenzamide

To a 250 ml flask fitted with reflux condensor containing 5-azido-2-chlorobenzoic acid and dry benzene (100 ml) was added freshly distilled thionyl chloride (12 ml) and the mixture warmed to initiate the reaction. On completion, the excess thionyl chloride and benzene was carefully removed using a water vacuum pump. To the residue was then carefully added cold concentrated ammonia solution (10 ml S.G. = 0.88). The white solid formed was washed with water (4 x 100 ml), dried and recrystallised from ethanol to give 5-azido-2-chlorobenzamide (9.g, 90%) (m.p. = 131-132°). (Found : C, 42.81; H, 2.56; N, 27.34, Cl, 18.20; $C_7H_5N_4OCl$ requires C, 42.90; H, 2.56; N, 27.34; Cl, 18.20; ν_{max} 3190 and 3460 (NH_2), 2130 (N_3), Mass spectrum m/e 196 (M^+).

Preparation of Methyl 5-azido-2-chlorobenzoate

Methyl 5-Nitro-2-chlorobenzoate

A solution of 5-nitro-2-chlorobenzoic acid (20g) in a 500 ml flask containing methanol (200 ml) and conc. H_2SO_4 (0.1 ml) and fitted with a reflux condenser, was refluxed for 48 hr. The methanol was removed and a white solid of methyl 5-nitro-2-chlorobenzoate was obtained. The yield was (80%)(m.p. = 70°)(lit [181] 73°).

Methyl 5-Amino-2-chlorobenzoate

The above nitro-ester (20g) in methanol (300 ml) was reduced with Raney-Nickel (10g) under hydrogen (50 ATMS) for 18h. after which the catalyst was removed by filtration and evaporation of the solvent gave a dark green oil of methyl 5-amino-2-chlorobenzoate (90%).

Methyl 5-azido-2-chlorobenzoate

In a 500 ml flask suspended in an ice-bath was added methyl 5-amino-2-chlorobenzoate (10g) and 50% HCl (100 ml) and the mixture cooled to 0°C. Diazotisation of this mixture followed by addition of the diazonium solution to a mixture of sodium azide (4g) and sodium acetate (50g) in water (50 ml) gave a dark yellow oil. This was then extracted with ether (200 ml), washed with 10% NaOH (2 x 50 ml), and then with water (2 x 50 ml) and finally dried over anhydrous magnesium sulphate. Evaporation of the ether followed by elution with light petroleum (b.p. = 40-60°) on alumina column gave white crystalline solid of methyl 5-azido-2-chlorobenzoate (8.9g) (m.p. = 30-31°) νmax 1740 (C=O), 2130 (N_3), Mass spectrum m/e 211 M^+, (Found : C, 45.24; H, 2.87; N, 20.01, Cl, 16.68; $C_8H_6N_3O_2Cl$ requires C, 45.41; H, 2.86; N, 19.86; Cl, 16.75).

Preparation of 2-Azidobenzophenone

2-Aminobenzophenone (8g) dissolved in 60 ml of 50% HCl was placed in an ice-bath and the mixture cooled to 0°C. To this was then added sodium nitrite (4g) in water (20 ml) and the mixture was stirred for 10 mins. This solution was then added dropwise to a solution containing sodium azide (5g) and sodium acetate (80g) in water (100 ml). The mixture was then extracted with ether (2 x 50 ml) washed with water and then dried over anhydrous Mg SO_4. The ether was then removed by evaporation and the oily contents preabsorbed into alumina and eluting with ether gave a pale yellow liquid of 2-azidobenzophenone (7.6g 85%). A portion was chilled in dry ice and methanol to give yellow plates (m.p. = 37°) (lit [12] 37-38°).

Thermolysis of the o-Azido-carbonyl Compounds

Decomposition of Methyl o-azidobenzoate in Bromobenzene

Methyl o-azidobenzoate (3g) in bromobenzene (30 ml) contained in a 250 flask was heated at 140° under nitrogen for 2h. after which the bromobenzene was removed by distillation under reduced pressure. The dark mass was then preabsorbed into alumina and eluting with light petroleum (b.p. 60-80°) gave 2,2'-bis (methoxycarbonyl)azobenzene (0.12g 4%) (m.p. = 101) (lit [188] m.p. = 101). Eluting with ether gave methyl anthanilate (0.1g 6%) which gave identical infrared spectrum with an available sample and finally, with an ether-methanol mixture (19:1), gave tars.

Thermolysis of Phenyl o-azidobenzoate in Bromobenzene

Phenyl o-azidobenzoate (3 gm) in bromobenzene was thermolysed at 140°C for 4h. The work up was similar to the previous experiment. Eluting with ether gave Bis-2,2'-(phenyoxycarbonyl) azobenzene (1%) (m.p. = 170) (lit [189] m.p. = 171). Eluting with ethanol gave polymeric materials.

Thermolysis of N-(2-azidobenzoyl) aniline in 1,2 dichlorobenzene

N-(2-azidobenzoyl)aniline (1g) in 1,2 dichlorobenzene (20 ml) was heated at 150° for 6h. in 250 ml flask. The solvent was removed by vacuum distillation and the black mass was eluted with ether-methanol mixture (19:1) on an alumina column to give polymeric materials.

Thermolysis of 2-Azidobenzamide in 1,2 dichlorobenzene

2-Azidobenzamide (3g) in 1,2 dichlorobenzene (30 ml) was heated under reflux at 150° for 5h. The solvent was removed under reduced pressure and the dark mass was eluted on alumina column with ether-methanol mixture (19:1) to give tars.

Thermolysis of 2-Azidobenzoic Acid in Bromobenzene

o-Azidobenzoic acid (2g) in bromobenzene (20 ml) was heated at 145° for 6h. The solvent was removed under reduced pressure and the tarry mass preabsorbed onto alumina. Eluting with ether-methanol mixture (19.1) gave tars.

Thermolysis of 2-Azidophenylthioester in Bromobenzene

2-Azidophenylthioester (2g) in bromobenzene was thermolysed in the usual apparatus at 140° for 3h. Removal of the solvent under reduced pressure left a dark red mass which was then columned on alumina with light petroleum (b.p. 60-80°) to give diphenyl disulphide (0.2g) (m.p. = 58°).

Eluting with ether gave a red polymeric material.

Thermolysis of Methyl o-azidobenzoate in m-Cresol

Methyl o-azidobenzoate (3g) in m-cresol (30 ml) was heated under reflux for 3h. in a 250 ml flask. The mixture was then carefully distilled at 182° to give aniline (40%). The remaining oily mass was then poured into a 10N. NaOH solution (50 ml) and the mixture vigorously stirred. This was then extracted with chloroform (100 ml) and then dried over anhydrous magnesium sulphate. The chloroform was then removed and elution of

the remaining dark mass on an alumina column with ether-methanol mixture (19:1) gave tars.

Thermolysis of Phenyl Azide in Cyclohexanol

Phenyl azide (3g) in cyclohexanol (30 ml) was heated under reflux for 3hrs. The solvent was removed under reduced pressure and the dark mass was columned on alumina with light petroleum (b.p. 40-60°) to give azobenzene (0.46g, 10%) (m.p. = 68) and with ether to give aniline (0.73g 30%) identified by comparison of infrared spectrum of authentic sample. Further elution of the column with ether-methanol mixture (19:1) gave tars.

Thermolysis of Methyl o-azidobenzoate in Cyclohexanol

Methyl o-azidobenzoate (3g) in cyclohexanol (30 ml) was heated under nitrogen at 140° in a 250 ml flask for 6h. The solvent was then removed by vacuum distillation and the brown oil was preabsorbed onto alumina. Eluting with light petroleum (b.p. 60-80°) gave (0.84g 20%) 2-cyclohexyloxy-3-methoxycarbonyl-3H-azepine (b.p. = 127° at 0.1 mm). ν_{max} 1750 (CO), 1620 (C=N), (Found : C, 67.54; H, 7.311; N, 5.80; $C_{14}H_{18}NO_3$ requires C, 67.72; H, 7.31; N, 5.64), $\tau(CCl_4)$; 2.9-3.1 (7H, d,), 3.4-4.5 (4H, 5H, 6H, m), 6.22 (OMe, s), 7.1-7.2 (3H, d,), 8.1-8.9 (C_6H_{10}, m). Mass spectrum m/e 248 (M^+), 189 ($M^+ - CO_2Me$). Eluting with ether gave methyl anthranilate (1.54g 60%) characterised by identical infrared spectrum with authentic sample and with ether-methanol (19.1) gave tars.

Photolysis of o-Azido Compounds in Alcohols

Photolysis of N-(2-Azidobenzoyl)aniline in Methanol

A solution of N-(2-azidobenzoyl)aniline (1g) in methanol (100 ml) was photolysed with a 125 W. medium pressure lamp (with pyrex filter) in an Hanover photochemical reactor for 24h. The methanol was removed on a rotary evaporator and the dark mass was preabsorbed onto alumina and then packed on top of an alumina column. Eluting with benzene-ether mixture (1:1) gave the anilide of 2-methoxy-3H-azepine-3-carboxylic acid (0.61g, 60%) m.p. = 159° νmax 3290 (NH) 1665 (CO), 1615 (C=N), Mass spectrum m./e 242 (M^+) λmax (EtOH.) 256 nm ($\log_\varepsilon$ 3.63), (Found : C, 69.30; H, 5.84; N, 11.70; $C_{14}H_{14}N_2O_2$ requires C, 69.41; H, 5.82; N, 11.59), τ($CDCl_3$) 6.54 (3H d) 6.25 (OMe, s); 3.3-4.2 (4H, 5H, 6H, m); 2.9-3.1 (7H, d) and 2.2-2.8 (aromatic protons, m).

Eluting with ether gave a trace of methyl anthranilate characterised by identical infrared spectrum of authentic sample and with ether-methanol mixture (19:1) gave tars.

Photolysis of N-(2-Azidobenzoyl)aniline in Ethanol

The procedure and work up was identical to the previous experiment. Eluting with light petrol (b.p. 40-60°) and ether mixture (1.1) gave the anilide of 2-ethoxy-3H-azepine-3-carboxylic acid (0.41g 40%) m.p. = 111° as a white solid. νmax 3290 (NH), 1670 (CO) 1610 (C=N), Mass spectrum m/e 256 (M^+). (Found : C, 70.64; H, 5.91; N, 11.01; $C_{15}H_{16}N_2O_2$ requires C, 70.57; H, 5.92; N, 10.97); τ($CDCl_3$) 3.2-4.3 (4H, 5H, 6H, m); 6.3-6.4 (3H, d), 2.9-3.05 (7H, d), 5.5-6.0 (CH_2 q), 8.6-8.8 (CH_3, t), 2.0-2.7 (aromatic, m). Eluting with ether-methanol mixture (19:1) gave tars.

Photolysis of 2-Azidobenzamide in Ethanol

2-Azidobenzamide (1 gm) in ethanol (100 ml) was photolysed in the usual apparatus for 18h. The ethanol was removed on a rotary evaporator and the dark mass preabsorbed onto alumina. Eluting with ether gave 2-ethoxy-3H-azepine-3-carboxamide (0.90 g 81%) (m.p. = 153°C) as white plates. (Found : C, 59.60; H, 6.49; N, 15.59); $C_9H_{12}N_2O$ requires C, 59.90; H, 6.50; N, 15.55). νmax 3300 and 3200 (NH_2), 1670 (CO), 1615 (C=N) λmax (EtOH) 255 nm. ($\log_\varepsilon$ 3.65) τ($CDCl_3$), 2.9-3.1 (7H, d), 3.3-4.3 (4H, 5H, 6H, m), 6.5-6.6 (3H, d), 5.6-6.0 (CH_2, q), 8.3 (NH_2) removed by D_2O 8.7-9.0 (CH_3, d). Mass spectrum m/e 180 (M^+). Eluting with ether-methanol (19:1) gave polymeric materials.

Photolysis of 2-Azidobenzamide in N-Propanol

The procedure was identical to that of the previous experiment. Eluting with ether gave 2-(n-propoxy)-3H-azepine-3-carboxamide (0.73g, 67%) as a white solid. Recrystallisation from a light petrol (b.p. 40-60°) - ether (20:80) gave white plates (m.p. = 122°). (Found : C, 61.84; H, 7.26; N, 14.52; $C_{10}H_{14}N_2O$ requires C, 61.89; H, 7.27; N, 14.42); νmax 3380 and 3200 (NH_2), 1670 (C=O), 1610 (C=N). Mass spectrum m/e 194 (M^+); τ ($CDCl_3$), 2.9-3.1 (7H, d), 3.5-4.5 (4H, 5H, 6H, m), 5.9-6.2 (CH_2, q), 6.5-6.7 (3H, d), 8.0-8.7 (CH_2 m), 9.0-9.3 (CH_3, t), 8.1 (NH_2) removed by D_2O. Further elution with ether-methanol (19.1) gave tars.

Photolysis of N-(2-azidobenzoyl)-o-anisidine in Ethanol

N-(2-azidobenzoyl)-o-anisidine (1g) in ethanol (100 ml) was photolysed in the usual apparatus for 24h. The ethanol was removed on a rotary evaporator and the dark mass columned on alumina with ether to give the o-anisidide of 2-ethoxy-3H-azepine-3-carboxylic acid as white plates (0.58g, 54%) (m.p. = 150), ν max 3300 (NH), 1670 (C=O), 1620 (C=N), Mass spectrum, m/e 270 (M^+), τ ($CDCl_3$) 2.1-2.8 (aromatics, m), 2.9-3.1 (7H, d), 3.3-4.3 (4H, 5H, 6H, m), 5.6-5.9 (CH_2, q), 6.1-6.25 (3H, d), 7.8 (CH_3, s), 8.7-8.95 (CH_3, t), (Found : C, 71.07; H, 6.70; N_3 10.32; $C_{16}H_{18}N_2O_2$ requires C, 71.00; H, 6.71; N, 10.36). Eluting with ether-methanol mixture gave tars.

Photolysis of Methyl o-azidobenzoate

a) Methanol

Methyl o-azidobenzoate (1g) in methanol (100 ml) was photolysed in the usual apparatus with pyrex filter for 24h. The methanol was removed on a rotary evaporator and the dark brown oil preabsorbed onto alumina. Elution of the column with light petroleum (b.p. 40-60) gave unreacted azide (0.1g) and with benzene gave 2-methoxy-3-methoxycarbonyl-3H-azepine (0.6g 58%) (b.p. 75° at 0.5 m.m. as a colourless oil). ν max 1740 (CO), 1620 (C=N), λ max (EtOH), 257n.m. ($\log_\varepsilon$ 3.75); mass spectrum m/e 181 $^+$ (M^+), 149 ($M^+ - CH_3OH$), 122 ($M^+ - 59$), (Found : C, 59.56; H, 6.07; N, 7.81; $C_9H_{11}N\,O_3$ requires C, 59.66; H, 6.12, N, 7.73, τ(CCl_4), 6.21 and 3.31 (2(OMe), 2 s), 3.4-4.4 (4H, 5H, 6H, m), 2.9-3.1 (7H,d) ($J_{6,7}$ 7.5 Hz) 7.1 (3H, d). Eluting with ether-methanol (19.1) gave polymeric materials.

b) Ethanol

The procedure was identical to the previous experiment. Eluting with benzene gave 2-ethoxy-3-methoxycarbonyl-3H-azepine (0.7g 67%) (b.p. 120° at 4 m.m.). (Found : C, 61.61; H, 6.70; N, 7.09; $C_{10}H_{13}O_3N$ requires C, 61.53; H, 6.71; N, 7.18); mass spectrum m/e 195 (M^+), ν max 1740 (C=O), 1620 (C=N), $\tau(CCl_4)$, 6.21 (OMe, s), 3.5-4.8 (4H, 5H, 6H, m), 7.2 (3H, d), 8.88 (CH_3, t), 5.7-5.95 (O-CH_2-CH_3, oct); 2.8-3.0 (7H, d) ($J_{6,7}$ 7.5 Hz). Eluting with ether gave a trace of methyl anthanilate characterised by identical infrared spectrum with authentic sample and with ether-methanol (19.1) mixture gave tars.

c) Propanol

As for previous experiments. Eluting with benzene gave 2-(n-propoxy-3-methoxy carbonyl-3H-azepine) (0.75g 66%) (b.p. = 130°C at 1 mm as a colourless oil). νmax 1750 (CO), 1630(C=N), mass spectrum m/e 209 (M^+), 108^+ base peak ($M^+ - 59 + 42$). (Found : C, 63.24; H, 4.24; N, 6.70; $C_{11}H_{15}O_3N$ requires C, 63.14; H, 7.23; N, 6.73), $\tau(CCl_4)$, 6.2 (OMe, s), 3.4-4.5 (4H, 5H, 6H, m), 7.1-7.2 (3H, d), 2.9-3.1(7H, d) ($J_{6,7}$ 7.5 Hz), 9.1(CH_3, t), 8.1-8.65 (-CH -q), 5.75-6.1 (-O-CH, sext). Eluting with ether-methanol mixture (19.1) gave polymeric materials.

d) Isopropanol

As previous experiments. Eluting with benzene gave 2-(isopropoxy)-3-methoxycarbonyl -3H-azepine as a colourless oil (0.85g 72%) (b.p. = 100° at 0.3 mm). (Found : C, 63.01; H, 7.18; N, 6.71; $C_{11}H_{15}N\,O_3$ requires C, 63.14; H, 7.23; N, 6.73). Mass spectrum m/e 209 (M^+) $\tau(CCl_4)$, 2.9-3.1 (7H, d), 3.5-4.5

(4H, 5H, 6H, m), 6.21 (OMe, s), 8.7-8.85 ($C(CH_3)_2$,q) and 4.65-5.35 (OCH sept) 7.15 (3H,d). νmax 1740 (CO), 1620 (C=N). Eluting with ethanol gave tars.

e) N-Butanol

Eluting with benzene gave 2-(n-butoxy-3-methoxycarbonyl 3H-azepine as a colourless oil (0.74g 59%) (b.p. 110° at 0.1 mm) $\tau(CCl_4)$ 6.22 (OMe, s), 2.9-3.1 (7H, d), 3.5-4.5 (4H, 5H, 6H, m) 7.15 (3H, d), 8.0-9.2 (CH_2-CH_2-CH_3, m), 5.6-6.1 (-O-CH_2-, m). Found C, 64.64; H, 7.64; N, 6.36; $C_{12}H_{17}N\,O_3$ requires C, 64.55, H, 7.68; N, 6.27), ν max 1745 (C=O), mass spectrum m/e 223 (M^+). Eluting with ether gave a trace of methyl anthaniate characterised by comparison with authentic sample and with ether-methanol mixture (19.1) gave tars.

Photolysis of Phenyl o-azidobenzoate in Methanol

Phenyl o-azidobenzoate (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. The methanol was removed and the oily mass was preabsorbed onto alumina which was then packed onto an alumina column. Elution of this column with benzene gave 2-methoxy-3-phenoxycarbonyl-3H-azepine as a pale yellow oil (0.61g, 59%) (m.p. = 115° at 0.3 m.m.) νmax 1750 (CO), 1620 (C=N), mass spectrum m/e 243 (M^+) base peak 122$^+$ (M^+ - $PhCO_2$), $\tau(CCl_4)$ 2.2-3.2 (aromatics, m); 3.3-4.2 (4H, 5H, 6H, m), 6.21 (OMe, s), 6.6-6.7 (3H, d) (Found : C, 69.30; H, 5.38; N, 5.84; $C_{14}H_{13}N\,O_3$ requires C, 69.13; H, 5.39; N, 5.76). Eluting with ether-methanol mixture (19.1) gave tars.

Photolysis of Methyl 2-azido-4-chlorobenzoate in Methanol

Methyl 2-azido-4-chlorobenzoate (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. The methanol was then removed on a rotary evaporator and the oily mass was distilled under vacuum in a Kugelrohri to give 2-methoxy-3-methoxycarbonyl -7-chloro-3H-azepine as a pale yellow oil (0.7g 69%) (b.p. 120° at 0.2 mm). ν_{max} 1745 (C=O), 1620 (C=N); mass spectrum m/e 215 (M^+) 122, base peak (M^+ - Cl - CO_2 Me). (Found : C, 50.24; H, 4.66; N, 6.46; Cl, 16.41; $C_9H_{10}NO_3Cl$ requires C, 50.13; H, 4.67; N, 6.50; Cl, 16.44), $\tau(CCl_4)$ 5.8 and 5.9 (2(OMe), 2 s); 6.7 (3H, d), 3.1-4.1 (4H, 5H, 6H, m). The dark mass left behind was dissolved in ethanol and preabsorbed onto alumina and eluting with ether-methanol mixture (19.1) gave polymeric materials.

Photolysis of 2-Azidobenzophenone in Methanol

2-Azidobenzophenone in methanol (100 ml) was photolysed for 36 hrs. in the usual apparatus (with pyrex filter). The methanol was removed and the dark oil preabsorbed onto alumina. Elution of the column with a light petroleum (b.p. 60-80°)-benzene mixture (1:3) gave 3-benzoyl-2-methoxy-3H-azepine (0.10g 11%) (m.p. = 66°) (lit [14] 66-68°). Elution with benzene gave 2-phenylanthranil (0.34g, 37%) m.p. = 53° (lit [14] 53°) and with ether-methanol mixture (19.1) gave tars.

Photolysis of 2-Azidobenzoic Anhydride in Methanol

2-Azidobenzoic anhydride (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. The methanol was removed on a rotary evaporator and the dark oil columned over alumina with light petroleum (b.p. 40-60°) to give methyl benzoate (0.1g, 20%) characterised by comparison of infrared spectrum with authentic sample and with benzene to give 2-methoxy-3-methoxy-carbonyl-3H-azepine (0.2g 35%). Eluting with ethanol gave tars.

Photolysis of 2-Azidophenylthioester in Methanol

2-Azidophenylthioester (1g) in methanol (100 ml) was photolysed in the usual manner for 48 hr. Removal of the methanol left a dark oil which was columned on alumina with light petroleum (b.p. 40-60°) to give diphenyl disulphide. m.p. = 58. Eluting with ether gave a dark red polymer from which no other products could be characterised.

Photolysis of 2-Azidobenzoic Acid in Methanol

2-Azidobenzoic acid (1g) in methanol (100 ml) was photolysed in the usual apparatus for 48h. Removal of the ethanol left a dark mass which was columned on silica with benzene to give unreacted starting materials (0.2g) and with ether/methanol mixture (19:1) to give tars.

Photolysis of 5-Azido-2-chlorobenzoic Acid in Methanol

Using the same quantities and reaction conditions as above and eluting with ether-methanol mixture (19:1) gave tars.

Photolysis of Methyl 5-azido-2-chlorobenzoate in Methanol

Methyl 5-azido-2-chlorobenzoate (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. Removal of the solvent followed by elution of the oily material on alumina column with ether-methanol mixture (19.1) gave tars.

Photolysis of Methyl 4-azidobenzoate in Methanol

Methyl 4-azidobenzoate (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. Removal of the solvent on a rotary evaporator followed by elution of the residue on alumina with ether gave methyl 4-aminobenzoate (0.24g, 28%)(m.p. = 111°) (lit [127] 112°). Further elution of column with ether-methanol mixture (19.1) gave tars.

Photolysis of 5-Azido-2-chlorobenzamide

The concentrations, conditions, and time of photolysis was similar to the previous experiment and elution of the tarry mass on alumina column with ether-methanol mixture (19.1) gave tars.

The Photolysis of Methyl o-azidobenzoate in an Acetophenone-Methanol Mixture

Methyl o-azidobenzoate (1g) was photolysed in a mixture containing methanol (50 ml) and acetophenone (50 ml) for 30h. The solvents were removed by distillation under reduced pressure and the dark oil residue was columned on alumina with benzene to give 2-methoxy-3-methoxycarbonyl -3H-azepine (0.22g 20%) and methyl anthranilate (0.44g, 60%) both of which were confirmed by comparison of infrared spectra of authentic samples.

Photolysis of Phenyl azide in Methanol

Phenyl azide (1g) in methanol (100 ml) was photolysed in the usual apparatus for 24h. The methanol was removed on a rotary evaporator and the oily residue was columed with ether on alumina to give aniline (0.47g 60%) confirmed by comparison with infrared spectrum of authentic sample and with ether-methanol mixture to give tars.

Photolysis of Phenyl azide in Cyclohexanol

Phenyl azide (1g) in cyclohexanol (100 ml) was photolysed under the usual conditions for 30h. The mixture was then poured in 100 ml of 10% NaOH and then extracted with ether (2 x 100 ml). It was then washed with water (3 x 50 ml), and then dried over anhydrous magnesium sulphate. Removal of the ether followed by elution of dark oil on alumina column with ether gave aniline (0.29g, 30%) confirmed as above and with ether-methanol (19.1) gave tars.

Part 3

Preparation of 2-Azidoaniline

a) N-(o-nitrophenyl)succinimide

o-Nitroaniline (13.8g; 0.1 mol) and succinic anhydride (10g; 0.1 mol) was heated together at 200° for 1 hr. in an open flask. The dark pasty mixture was then run into a mortar where it solidified. It was then ground into a powder and transferred to a sinter and washed with toluene (4 x 50 ml). It was then recrystallised from ethanol to give a pale yellow solid of N-(o-nitrophenyl) succinimide (15g) (m.p. = 157°) (lit[142] 156°).

b) N-(2-aminophenyl)succinimide

A solution of N-(2-nitrophenyl) succinimide (0.2 mol) in N,N'-dimethylformamide (400 ml) was hydrogenated with 5% palladium on charcoal (5g) in a baskerville for 12h. The mixture was filtered to remove the catalyst and the solvent removed under reduced pressure. The pale brown solid was then triturated with ethanol (30 ml) and then filtered to yield N-(2-aminophenyl)succinimide (36g, 92%) (m.p. = 237-238°) (lit[142] 237°).

c) N-(2-azidophenyl) succinimide

A solution of N-(2-aminophenyl) succinimide (19g) in concentrated hydrochloric acid (100 ml) and water (500 ml) was cooled to 0°. This solution was then diazotised by slow addition of sodium nitrite (8g) in water (50 ml). The diazonium solution was then run into a litre flask containing sodium azide (8g) and sodium acetate (100 g) in water (100 ml) and the mixture stirred. The white solid formed was filtered, washed with water (2 x 100 ml),

dried and then recrystallised from ethanol to give white plates of N-(2-azidophenyl) succinimide (20.6g, 94%) (m.p. = 141°) (lit [42] 142°).

d) 2-Azidoaniline

A mixture of N-(2-azidophenyl)succinimide (5g) in 10% sodium hydroxide (500 ml) was stirred at 70° for 3h. The mixture was cooled and extracted with dichloromethane (3 x 200 ml), dried over anhydrous magnesium sulphate, and then decoloured with charcoal. Removal of the solvent gave 2-azidoaniline (2.5g) which was then recrystallised from light petroleum (b.p. 60-80°) to give pale yellow needles (m.p. = 62-63°) (lit [42] 63°)

Preparation of 2-Azidoacetanilide

o-Azidoaniline (3g) was added to acetic anhydride (15 ml) in a 100 ml flask and the mixture heated on a water bath for 30 mins. To this was then added water (10 ml) and the solution heated on a water bath for a further 10 mins. The solution was then poured into a 250 ml containing ace and the mixture stirred. The pale brown solid formed was filtered, washed with water (2 x 100 ml) and dried. Recrystallisation from aqueous ethanol gave 2-azidoacetanilide (3.5g, 89%) (m.p. = 87°) as a white flakes. ν_{max} 3250 (NH), (C=O), 2140 (N_3). Mass spectrum m/e 176 (M^+); (Found : C, 54.94; H, 4.60; N, 32.04; $C_8H_8N_4O$ requires C, 54.85; H, 4.60; N, 31.98).

Preparation of 2-Azidobenzanilide

To 2-azidoaniline (3g) and pyridine (20 ml) contained in a 100 ml flask was added benzoyl chloride (6g) and the mixture thoroughly shaken for 5 mins after which the contents of the flask

were poured into water (100 ml) in a 250 flask. The dark brown solid formed was filtered, washed with 4N.HCl (2 x 50 ml); 4N.NaOH (2 x 50 ml) and water (2 x 25 ml) and then dried. Recrystallisation from aqueous ethanol gave 2-azidobenzanilide (5g, 93%) (m.p. = 86 -87°) as white feathery crystals. ν_{max} 3220 (NH), 2130 (N_3), 1650 (CO); mass spectrum m/e 238 (M^+); (Found : C, 65.39; H, 4.22; N, 23.41; $C_{13}H_{10}N_4O$ requires C, 65.54; H, 4.23; N, 23.52).

Preparation of 2-Azido-N-(p-tosyl)aniline

2-Azidoaniline (3g) in pyridine (20 ml) was placed in a 100 ml conical flask and p-toluenesulphonyl chloride (4g) was added to it and the mixture warmed on a water bath for 10 mins after which the contents of the flask were poured into a beaker containing water (100 ml). The solid formed was washed with 4N.HCl and 4N.NaOH solutions as in the previous experiment, dried and recrystallised from aqueous ethanol to give 2-azido-N-(p-tosyl)aniline (4.5g, 70%) (m.p. = 130-140°) as a white solid. ν_{max} 3250 (NH), 2140 (N_3); mass spectrum m/e 288 (M^+); (Found : C, 53.99; H 4.20; N, 19.44 S, 11.01; $C_{13}H_{12}N_4O_2S$ requires C, 54.15; H, 4.20; N, 19.43; S, 11.12).

Preparation of N-(2-Azidophenyl) urea

2-Azidoaniline (3g) and 50% glacial acetic acid (20 ml) were added to a 250 ml flask and the solution warmed to dissolve the amine. To this was then added sodium cyanate (2g) in water (20 ml) dropwise and on completion the solution was left to stand whereupon a pale yellow solid was formed. This was then filtered, washed with water and then dried. Recrystallisation from light

petroleum (b.p. 40-60°)/ethanol mixture (1:1) gave white plates of N-(2-azidophenyl)urea (3.1g, 78%) (m.p. = 170°). ν_{max} 3500 and 3350 (NH_2), 3200 (NH), 2140 (N_3) and 1670 (C=O); mass spectrum m/e 177 (M^+); (Found : C, 47.51; H, 3.96; N, 39.18; $C_7H_7N_5O$ requires C, 47.32; H, 3.97; N, 39.41).

Preparation of N-(2-Azidophenyl)-N'-phenylurea

a) Anthranilohydrazide

In a 100 ml round bottom flask and heated under reflux for 2h. was a solution containing hydrazine hydrate (24 ml) and methyl anthranilate (20 g) in ethanol (20 ml). The mixture was then cooled and the white crystalline solid was filtered and then washed with cold ethanol (2 x 25 ml) and then dried. The yield was 17g (85%) (m.p. = 124°).

b) 2-Aminobenzoyl Azide

The method was based on that of Rees and his co-workers.[145]

2-Aminobenzhydrazide (11.3g) was dissolved in a mixture of glacial acetic acid (20 ml) and water (35 ml) and sodium nitrite (7g) in water (40 ml) was added dropwise to this solution at 0°C. The yellow solid formed was filtered and then washed with water (30 ml). This precipitate was then stirred with ethanol (2 x 50 ml) in a 250 ml beaker and the solid left in solution was filtered. The ethanolic solution was then poured into 500 ml of water and slowly a pale yellow solid crystallised out of solution. When this was complete, the solid was filtered and dried. This was sufficiently pure for the next stage. The yield was 4.5g (m.p. = 76°)

c) 2-Azidobenzoyl Azide

2-Aminobenzoyl azide (4.5g) was added to 50 ml of a 50% hydrochloric acid and this was diazotised with sodium nitrite (1.5g) in water (20 ml) under the usual conditions. The diazonium solution was then added dropwise to a cold solution containing sodium azide (1.2g) and sodium acetate (40g) in water (30 ml). The white solid formed was filtered, washed with water (2 x 25 ml) and then dried. It was then purified by dissolving it in dry ether and using an alumina column as a filter, followed by the reduction of the ether volume to about 10 ml. On standing white needles of 2-azidobenzoyl azide were formed. The yield was 2.9g (56%). ν max 2140 (N_3), and 1720 (C=O); Mass spectrum m/e 188 (M^+), 160 ($M^+ - N_2$), (Found : C, 45.60; H, 2.14; N, 44.63; $C_7H_4N_6O$ requires C, 45.41; H, 2.14; N, 44.67).

d) N-Phenyl-N'-(o-azidophenyl)urea

2-Azidobenzoyl azide (3g) and dry light petroleum (b.p. 40-60°) in a 100 ml flask fitted with reflux condensor was heated in a steam bath for 1 hr. after which freshly distilled aniline (2g) was added and the mixture stirred. A white solid was immediately formed which was filtered and dried. A pure sample of N-phenyl-N'-(o-azidophenyl)urea (3.8g 94%) (m.p. = 174° decomposition) was obtained as white crystals by recrystallisation from ether/light petroleum (b.p. 40-60°) mixture (4.1). νmax 3300 and 3280 (NH), 2125 (N_3) and 1650 (C=O); (Found : C, 61.48; H, 4.37; N, 27.51; $C_{13}H_{11}N_5O$ requires C, 61.55; H, 4.38; N, 27.67); mass spectrum m/e 253 (M^+).

Preparation of N-(2-Azidophenyl)-N'-(p-tolyl)urea

This was similar to the previous experiment and p-toluidine (2.1g) was added to the azido isocyanate/petrol mixture and this resulted in the formation of N-(2-azidophenyl)-N'-(p-tolyl)-urea as a white solid (recrystallised from aquious ethanol) (3.6g, 84%); (m.p. = 181°); ν_{max} 3310 and 3280 (NH), 2125 (N_3), 1650 (CO); mass spectrum m/e 267 (M^+); (Found : C, 62.83; H, 4.90; N, 26.16; $C_{14}H_{14}N_5O$ requires C, 62.91; H, 4.90; N, 26.20).

Preparation of Ethyl-N-(o-azidophenyl)carbamate

Method 1

a) From 2-Azidobenzoyl azide and Ethanol

2-Azidobenzoyl azide (3g) in absolute ethanol (50 ml) in a 250 ml flask was refluxed on a water bath for 1 hr. The ethanol was carefully removed on a rotary evaporator to leave a yellow oil. This was carefully preabsorbed onto alumina and eluting the alumina column with dry light petroleum (b.p. 40-60°) gave Ethyl-N-(o-azidophenyl) carbamate pale yellow oil (3.1g, 94%), mass spectrum m/e 206 (M^+), ν_{max} 3415 (NH), 2120 (N_3), and 1745 (C=O); $\tau(CCl_4)$ 2.8-3.1 (aromatics, m), 5.8-6.1 (CH_2, q) and 8.7-8.9 (CH_3, t); (Found : C, 52.51; H, 4.89; N, 27.24; $C_9H_{10}N_4O_2$ requires C, 52.42; H, 4.89; N, 27.17).

Method 2

b) From 2-Azidoaniline and Ethyl chloroformate

2-Azidoaniline (3g) in pyridine (20 ml) was added to a 100 ml flask and to this was then added ethyl chloroformate (4g) and the mixture warmed on a steam bath with constant stirring for 10 mins. It was then poured in a beaker containing 200 ml of water

and the mixture stirred. The oily layer which settled to the bottom of the flask was extracted with ether (100 ml) washed 2N.HCl (2 x 50 ml), water (2 x 200 ml), and then dried over anhydrous magnesium sulphate. Careful removal of the ether left a dark yellow oil which was purified as Method 1. The yield was 4.3g (93%).

Attempted Synthesis of Phenyl-N-(o-azidophenyl)carbamate

2-Azidoaniline (3g) in pyridine (20 ml) was added to a 100 ml flask and to this was added phenyl chloroformate (5g) and the procedure was as the previous experiment. However removal of the ether left a white solid which decomposed rapidly on exposure to the atmosphere to give a mixture of o-azidoaniline and phenol both of which were identified by comparison with known samples.

Preparation of N-(o-azidophenyl)-N'-phenylthiourea

2-Azidoaniline (3g) in 100 ml of light petroleum (b.p. 60-80°) was added to phenyl isothiocyanate (6g) in a 250 ml flask fitted with a reflux condensor. The mixture was refluxed in a steam bath for 30 mins. The white solid formed was filtered, washed with further light petrol (b.p. 60-80°) (2 x 50 ml) and recrystallised from ethanol to give N-(o-azidophenyl)-N'-phenylthiourea. as a white solid (m.p. = 120°). The yield was (5g 93%), νmax 3200 (NH), 2140 (N_3), 1200 (C=S); mass spectrum m/e, 269 (M^+); (Found : C, 57.94; H, 4.12; N, 25.89; S, 11.82; $C_{13}H_{11}N_5S$ requires C, 57.98; H, 4.12; N, 26.00; S, 11.90).

Thermolyses

Decomposition of 2-Azidoacetanilide in Bromobenzene

2-Azidoacetanilide (2g) in bromobenzine (20 ml) was heated under reflux at 140° in a 250 ml flask for 4h. after which the solvent was removed by distillation under vacuum. The dark mass was then eluted with ether on an alumina column to give N-acetyl-o-phenylenediamine (0.31g 12%) m.p. = 132° (lit [190] 130°). Eluting with ether-methanol (19.1) mixture gave polymeric materials.

Decomposition of 2-Azidobenzanilide in Bromobenzene

2-Azidobenzanilide (3g) in bromobenzene (30 ml) was heated under reflux at 140° in a 250 ml flask for 4h. The solvent was removed by distillation under vacuum and the tarry mass was eluted with ether on alumina to give N-benzoyl-o-phenylenediame (0.24g 9%) (m.p. = 140°) (lit [198] m.p. = 141-142°). Further elution of the column with ethanol gave tars.

Decomposition of 2-Azido-N-(p-tosyl)aniline in Bromobenzene

2-Azido-N-(p-tosyl)aniline (3g) in bromobenzene was heated under reflux at 150° for 2h. The solvent was removed as the previous experiment and elution of the tarry mass with ether-methanol mixture (19.1) gave polymeric materials.

Decomposition of N-(2-azidophenyl)urea in 1,2 Dichlorobenzene

N-(2-azidophenyl)urea (2g) in 1,2 dichlorobenzene (20 ml) was heated under reflux in a 100 ml round bottom flask for 6h. The work up procedure was similar to the previous experiment and eluting the alumina column with ether-methanol mixture (19.1) gave tars.

Decomposition of N-phenyl-N'-(o-azidophenyl)urea in 1,2-Dichlorobenzene

N-phenyl-N'-(o-azidophenyl)urea (3g) in 1,2 dichlorobenzene (30 ml) was heated under reflux at 150° for 5 hr. The solvent was removed under reduced pressure and the black mass was columned on alumina with ether-methanol mixture (19.1) to give N,N'-diphenylurea (0.25g 10%) (m.p. = 238°). Further elution of the column with ethanol gave tars.

Decomposition of N-(o-azidophenyl)-N'-(p-tolyl)urea in 1,2 Dichlorobenzene

The procedure was identical to the previous experiment. The tarry mass from the 10% azide decomposition, was once again columned on alumina and eluting with ether-methanol mixture (19.1) gave N-phenyl-N'-(p-tolyl)urea (0.7g 30%) (m.p. = 213°). Eluting with ethanol gave polymeric materials.

Decomposition of 2-Azidoaniline in Chlorobenzene

2-Azidoaniline (3g) in chlorobenzene (30 ml) was heated under reflux at 120° for 3 hr. The work up was as the previous experiments and elution of the tarry mass on alumina with ether-methanol mixture gave tars.

Decomposition of Ethyl N-(o-azidophenyl)carbamate in Chlorobenzene

Ethyl N-(o-azidophenyl)carbamate (3g) in chlorobenzene (30 ml) was heated under reflux at 130° for 6h. The solvent was removed under vacuum and as usual elution of the alumina colum with light petroleum (b.p. 60-80°) gave BIS-2,2'-(ethylcarboxy-amino) azobenzene (3.9g 75%) (m.p. = 176°). ν_{max} 3400 (NH),

1725 (CO), mass spectrum m/e 356 (M^+). (Found : C, 60.81; H, 5.65; N, 15.78; $C_{18}H_{20}N_4O_4$ requires C, 60.66; H, 5.66; N, 15.72), (CCl_4) 2.3-3.1 (aromatics, m.), 5.4-5.8 (CH_2, q), 8.4-8.6 (CH_3, t).

Further elution of the column with ether-methanol mixture (19.1) gave tars. However when a 5% azide solution was decomposed, the work up only gave the azo compound (1.92g 40%) plus tars.

Decomposition of 2-Azidobenzoyl Azide in Chlorobenzene

2-Azidobenzoyl azide (3g) in chlorobenzene (30 ml) was heated under reflux at 130° for 4h. The solvent was removed in the usual manner and the dark mass columned on alumina. Elution of the column with a benzene gave 1,2, dihydro-2-oxobenzimidazole (0.07 9%) (m.p. = 302) (lit [89] 305°). Further elution of the column with chloroform gave tars.

Decomposition of N-(o-Azidophenyl)succinimide in Bromobenzene

N-(o-azidophenyl)succinimide (3g) in bromobenzene (30 ml) was heated under reflux at 150 for 5h. The work up was similar to previous experiment and elution of the tarry mass on alumina with ether-methanol mixture (19.1) gave polymeric materials.

Decomposition of N-(o-azidophenyl)-N'-phenylthiourea in Bromobenzene

N-(o-azidophenyl)-N'-phenylthiourea (2g) in bromobenzene (20 ml) was heated under reflux at 105° for 3 hr. On cooling a white solid was formed. This was filtered, washed with cold ethanol (20 ml). Recrystallisation from ethanol gave benzimidazole-2-thione (0.67g 29%) (m.p. = 308°) (lit [192] 309°). The ethanolic-bromobenzene

filtrate was removed on a rotary evaporator using a water pump and the dark mass remaining was columned on alumina with ether to give aniline (8%) characterised by comparison of infrared spectrum of available sample. Further elution of the column with ethanol gave tars.

Synthesis of N-(o-aminophenyl)-N'-phenylthiourea

The synthesis of this thiourea was based on the method of Lellmann and Gurthner.[182] o-phenylenediamine (0.1 mol) and phenyl isothiocyanate (0.1 mol) in light petroleum (b.p. 40-60°) was refluxed on a steam bath for 1 hr. The solution was cooled, and the solid formed was filtered, washed with cold ether (50 ml) and dried to give N-(o-aminophenyl-N'-phenylthiourea (0.9g 90%) (m.p. = 169°).

Thermolysis of N-(o-aminophenyl)N'-phenylthiourea in Bromobenzene

N-(o-aminophenyl)-N'-phenylthiourea (3g) in bromobenzene (30 ml) was heated under reflux at 110° for 3 hr. The work up was similar to the azide decomposition and gave benzinidazole-2-thione (0.75g 52%) and aniline (1.08g 15%).

Photolyses

Photolyses of Ethyl N-(o-azidophenyl)carbamate in Methanol

Ethyl-N-(o-azidophenyl)carbamate (1g) in methanol (100 ml) was photolysed in the usual apparatus (with pyrex filter) for 24h. The ethanol was removed on a rotary evaporator and the dark red oil was columned on alumina with light petroleum (b.p. 60-80°) to give unreacted azide (0.92g). Further elution of the column with chloroform gave polymeric materials.

Photolysis of N-(2-azidophenyl)succinimide in Methanol

N-(2-azidophenyl)succinimide (1g) in methanol (100 ml) was photolysed under the usual conditions for 30h. The work up was similar to the previous experiment and elution of the alumina column with ether gave N-(o-aminophenyl)succinimide (0.26g, 30%) (m.p. = 236°) (lit[142] 237°). Further elution of the column with ethanol gave tars.

Photolysis of 2-Azidobenzoyl azide in Benzene

2-Azidobenzoyl azide (1g) in benzene (100 ml) was photolysed in the usual apparatus for 30h. The volume of the benzene was then reduced to about 10 ml and then preabsorbed onto alumina. Elution of the column with benzene gave 1,2.dihydro-2-oxobenzimidazole (0.13g 15%) (m.p. = 303°) (lit [89] 305°). Further elution of the column with chloroform gave tars.

Photolysis of 2-Azidoaniline in Methanol

o-Azidoaniline (1g) in methanol (100 ml) was photolysed for 30h. The solvent was removed on a rotary evaporator and the dark mass was once again columned on alumina. Eluting with ether gave a trace of o-phenylenediamine which was characterised by an identical infrared spectrum of an authentic sample. Further elution of the column with ether-methanol mixture (19.1) gave tars.

Photolysis of N-phenyl-N'-(o-azidophenyl)urea in Methanol

N-phenyl-N'-(o-azidophenyl)urea (1g) in methanol (100 ml) was photolysed for 48h. The solvent was removed in the usual manner and the brown mass columned on alumina with ether-methanol mixture (19.1) to give unreacted azide (0.95g).

Photolysis of N-(2-azidophenyl)-N'-(p-tolyl)urea in Methanol

The procedure was identical to the previous experiment and elution of the brown mass with ether-methanol mixture (19.1) in alumina gave unreacted starting materials (0.91g).

Photolysis of 2-Azidobenzanilide in Methanol

2-Azidobenzanilide (1g) in methanol (100 ml) was photolysed in the usual apparatus for 30h. The methanol was removed as usual and the dark mass was columned on alumina with ether to give N-benzoyl-o-phenylenediamine (0.42g 17%) (m.p. = 140°) (lit [191] 141-142°). Further elution of the column with ethanol gave polymeric materials.

Part 4

Preparation of o-azidophenol.

This was based on the method of Foster and Fierz.[193]

o-aminophenol (20g) in water (200 ml) contained in a litre beaker was mixed with concentrated hydrochloric acid (50 ml) and the mixture was diazotised in the usual manner with sodium nitrite (10g) in water (50 ml). To this ice-cooled liquid was then added hydroxylamine hydrochloride (12.5g) in water (25 ml). This was then poured immediately into a 5-litre beaker containing ice-cooled water (800 ml) containing sodium carbonate (250g). A gas was liberated and the solution was then stirred for 12 hr. at $0^{\circ}C$.

The reaction mixture was then filtered and the filtrate was acidified with acetic acid (50 ml) and then extracted ether (3 x 100 ml). The dark coloured etheral solution was repeatedly agitated with a 8% sodium carbonate solution until the solution became faint pink, after which it was dried over anhydrous magnesium sulphate. To this etheral solution was then added 40% NaOH (30 ml). whereupon snow white crystals of the sodium salt were formed. This was then filtered. The free phenol was obtained by adding 4N. acetic acid, first forming an emulsion, which later solidified to produce colourless crystals of 2-azidophenol (14.86g 60%) (m.p. = 136°).

(N.B. excess acid should not be added in the later stage as the phenol will remain in solution).

Preparation o-Azidophenyl 2-azidobenzoate

2-Azidopherol (2.7g) in pyridine (20 ml) was mixed with o-azidobenzoyl chloride (3.8 g) in a 100 ml flask and the mixture was then poured in 200 ml of water contained in a 500 ml flask. The mixture was stirred vigorously whereupon a pale yellow solid was formed. This was filtered, washed with 5% NaOH solution (2 x 50 ml) and then with water (3 x 50 ml) and then dried. Recrystallisation from ethanol produced a white crystalline solid of o-azidophenyl 2-azidobenzoate. (5.3g, 90%) (m.p. = 66°) ν max 2110 (N_3), 1750 (CO), mass spectrum m/e 280 (M^+); (Found : C, 55.77; H, 2.88; N, 30.06; $C_{13}H_8N_6O_2$ requires C, 55.72; H, 2.88; N, 29.99).

Preparation N-(2-azidobenzoyl) o-azidoaniline

2-Azidoaniline (2.7g) in pyridine (10 ml) was benzoylated with o-azidobenzoyl chloride (3.6g) in a 100 ml flask. The mixture was then poured into water (100 ml) in a 250 ml flask and thoroughly stirred. The solid formed was filtered, washed with water (3 x 50 ml) and dried. Recrystallisation from ethanol produced a white solid of N-(2-azidobenzoyl) o-azidoaniline , (4.55g 81%) (m.p. = 113°), ν max 3290 (NH); 1650 (CO) and 2160 (N_3); mass spectrum m/e 279 (M^+). (Found : C, 55.90; H, 3.24; N, 35.18; $C_{13}H_9N_7O$ requires C, 55.91; H, 3.25; N, 35.11).

Preparation of N-N'-di(o-azidophenyl)urea

2-Azidoaniline (2.7) and 2-azidobenzoyl azide (3.8g) in light petroleum (b.p. 40-60°) was refluxed in a 100 ml flask on a steam bath. The white solid formed was filtered and then recrystallised from ethanol to give a white solid of N-N'-di

(o-azidophenyl)urea (5.33g 90%) (m.p. = 212°), νmax 3200 (NH), 2160 (N_3) and 1645 (CO), (Found : C, 52.99; H, 8.42; N, 38.12; $C_{13}H_{10}N_8O$ requires C, 53.06; H, 3.43; N, 38.08); mass spectrum m/e 294 (M^+).

Photolysis of 2-Azidophenyl-2'-azidobenzoate in Methanol

2-Azidophenyl-2'-azidobenzoate (1g) was photolysed in methanol (100 ml) in the usual apparatus (with pyrex filter for 72h. after which the methanol was removed on a rotary evaporator to give 0.98g of unreacted starting material. When a quartz filter was employed and the solution irradiated for 24h. and work up of the reaction as above followed by chromatography on alumina produced unreacted azide (0.6g) eluting with ether-methanol mixture (19.1) and with ethanol gave polymeric materials.

Photolysis of N-(2-azidobenzoyl)-o-azidoaniline

The procedure was the same as above in that irradiation for 48h. in methanol gave starting materials quantitatively whereas irradiation for 24h. with quartz filter gave unreactive starting material (0.5g) plus polymeric material.

Photolysis of N,N'-di(o-azidophenyl)urea in Methanol

The procedure was identical to the previous photolysis and irradation of the azide (1g) in methanol (100 ml) for 72h. followed by the removal of the solvent gave starting materials (0.95g).

Part 5

Reaction of Methyl o-azidobenzoate with Hydrazine

a) Hydrazine in 3 molar excess

In a 100 ml flask containing methanol (20 ml) and methyl o-azidobenzoate (3.26g) was added hydrazine hydrate (3.1g). An exothermic reaction occurred with the evolution of nitrogen and the solution smelt strongly of ammonia. The reaction was then allowed to stand overnight and poured into 200 ml of cold water and the mixture thoroughly stirred whereupon a pale yellow solid was formed which was filtered, washed with water (2 x 50 ml) and then dried. Recrystallisation from ethanol produced white rectangular plates of indazoline-3-one (1.88g 70%) (m.p. 245°) (lit [194] 242°).

b) Hydrazine in molar quantities

The reaction in this case was slow and was accelerated by refluxing in methanol for 10h. and removal of the solvent followed by t.l.c. showed that only indazoline-3-one and methyl-o-azidobenzoate were present.

Reaction of Methyl o-azidobenzoate with N-methylhydrazine

Methyl o-azidobenzoate (3.26g) in ethanol (20 ml) was added to N-methylhydrazine (3.0g) in a 100 ml flask fitted with reflux condensor and the mixture was refluxed for 10h. on a steam bath. The ethanol was then removed and the dark brown solid was columned on alumina with ether-methanol (18.2) mixture to give indazoline-3-one (1.90g 72%) (m.p. = 242°). This gave an identical infrared spectra to the sample produced from hydrazine hydrate.

Reaction of Methyl o-azidobenzoate with Phenylhydrazine

Methyl o-azidobenzoate (3.26g) in ethanol (20 ml) and phenylhydrazine (3.2g) was reflux in a similar apparatus as the previous experiment for 10 hr. The ethanol was removed on a rotary evaporator and t.l.c. on alumina with light petroleum (b.p. 60-80°) showed that only starting materials were present.

Reaction of Hydrazine Hydrate with Furan

To hydrazine hydrate (0.6g) in ethanol (10 ml) contained in a 100 ml flask was added furan (0.8g) and the mixture heated under reflux for 2 hr. Careful t.l.c. investigation on silica with light petroleum (b.p. 60-80°) indicated that only starting materials were present.

Reaction of Methyl o-azidobenzoate in Hydrazine Hydrate and Furan

To methyl o-azidobenzoate (1.63g) in methanol (10 ml) contained in a 100 ml flask was added hydrazine hydrate (1.5g) and furan (0.8g) and the mixture stirred at room temperature for 12h. The ethanol was removed and the mixture chromatographed on alumina. Apart from a trace of furan which was obtained by elution of the column with ether, further elution of the column with ether-methanol (19.1) mixture gave indazoline-3-one (0.7g).

The Reaction of Methyl o-azidobenzoate with Hydrazine to determine the amounts of Nitrogen and Ammonia evolved

To methyl o-azidobenzoate (1.63g) in ethanol (10 ml) contained in a conical flask and fitted with a gas outlet was added hydrazine hydrate (1.5g). The gases evolved was passed through 50 ml of 0.1M HCl to absorb the ammonia and then into a gas burette

to determine the volume of nitrogen. Evolution of nitrogen was steady for the first two hours but ceased after 10 hrs. The volume liberated was 500 cc which was equivalent to 2 moles of nitrogen. The 0.1M HCl solution was then back titrated with 0.1M NaOH and the weight of ammonia calculated i.e. (0.009g) which did not correspond to the evolution of 1 mole of ammonia.

Reaction of 2-Azidobenzoyl Chloride with N-methylhydrazine in Pyridine

To a solution of N-methylhydrazine (3g) in pyridine (20 ml) in a 100 ml flask suspended in an ice bath was added dropwise 2-azidobenzoyl chloride (1.8l). The mixture was stirred for a further 5 minutes and then poured into 200 ml of cold water contained in a 500 ml beaker. The solution was then left to stand whereupon a dark brown solid was formed which was filtered, washed with water (2 x 50 ml), and finally with aqueous acetone (20 ml). Recrystallisation from ethanol produced white plates of N(2-azidobenzoyl)-N'-(2-azidobenzoyl)-N-methylhydrazine (2.69g, 80%) (m.p. 142) ν max 3280 (NH), 2170 (N_3), 1690 (CO), 1640 (CO); mass spectrum m/e 336 (M^+); (Found : C, 53.71; H, 3.59; N, 33.28; $C_{15}H_{12}N_8O_2$ requires C, 53.57; H, 3.60; N, 33.32).

Reaction of 2-Azidobenzoyl Chloride with N-methylhydrazine in Ethanol

The reaction conditions were identical to that above with the only exception being that the reaction was carried out in ethanol. The solid formed after the removal of the ethanol was washed with water (2 x 50 ml) and recrystallisation from ethanol

produced N-(2-azidobenzoyl)-N'-(2-azidobenzoyl)-N-methylhydrazine (2.84g 85%) (m.p. = 143°).

Reaction of 2-Azidobenzoyl Chloride with Hydrazine Hydrate in Pyridine

To a solution of hydrazine hydrate (3g) in pyridine (20 ml) in a 100 ml flask and suspended in an ice-bath was added dropwise 2-azidobenzoyl chloride (1.8g). The mixture was worked up as the previous experiment (i.e. that of N-methylhydrazine in pyridine) and crystallisation from ethanol gave a white solid of N-(2-azidobenzoyl)-N'-(2-azidobenzoyl)hydrazine (2.24g 70%) (m.p. = 164°) νmax 3290 (NH), 2160 (N_3), 1660 (CO); mass spectrum m/e 322 (M); (Found : C, 52.01; H, 3.13; N, 34.65); $C_{14}H_{10}N_8O_2$ requires C, 52.17; H, 3.13; N, 34.76).

Reaction of 2-Azidobenzoyl Chloride with Hydrazine Hydrate in Ethanol

Like the previous experiment the procedure and work up was identical and recrystallisation from ethanol gave N(2-azidobenzoyl)-N'-(2-azidobenzoyl)hydrazine as an impure mixture. Attempts to separate the impurities by chromatography failed.

Reaction of 2-Azidobenzoyl Chloride and Phenylhydrazine in Pyridine

To a solution of phenylhydrazine (1.1g) in pyridine (20 ml) was added 2-azidobenzoyl chloride (1.8g). The mixture was then poured into 200 ml of cold water and then stirred whereupon an oil settled to the bottom of the beaker. It was left to stand for 4h. during which the oil solidified. It was then filtered, washed with

4 N.HCl (50 ml), water (2 x 50 ml) and then dried. The solid was then dissolved in hot ethanol (10 ml) and the solution decolourised with charcoal and filtered. To the clear filtrate was then added light petroleum (b.p. 60-80°) (5 ml) and the solution left to stand whereupon white needles of N-phenyl-N'-(o-azidobenzoyl) hydrazine (2.07g, 82%) (m.p. = 112°) was formed. (Found : C, 61.70; H, 4.38; N, 27.41; $C_{13}H_{11}N_{15}O$ requires C, 61.65; H, 4.38; N, 27.32) ν max 3370 (NH), 3310 (NH); 2150 (N_3), 1645 (CO); mass spectrum m/e 253 (M^+).

Reaction of Phenyl o-azidobenzoate with Hydrazine Hydrate

Phenyl o-azidobenzoate (2.4g) in ethanol (20 ml) was added to hydrazine hydrate (2g) and the mixture left to stand for 12 hr. The ethanol was removed and the dark solid was columned on alumina with ether-methanol mixture (19.1) to give indazoline-3-one (0.95g 70%). Eluting with ethanol gave phenol (0.19g, 20%) which was characterised by mixed melting (m.p. = 45°) point with authentic sample.

Synthesis of the Ethyl ester of 2-Azidophenylacetic Acid

The ethyl ester of 2-nitrophenylacetic acid (8.4g) in benzene (300 ml) was reduced under atmospheric conditions with palladium charcoal (1g) in the presence of hydrogen for 10 hr. The solution was then filtered to remove catalyst. Removal of the solvent with gently heating in a rotary evaporator resulted in the formation of oxindole (3.7g, 70%) (m.p. = 124°) (lit [195]). This problem was overcome not by the isolation of the amino-ester but by

its conversion to the hydrochloride salt. This was done by adding 50% HCl solution (40 ml) to the benzene solution and the mixture thoroughly shaken. The aqueous layer was then extracted and then diazotised in the usual manner and then treated with sodium azide to give the ethyl ester of 2-azidophenyl acetic acid (7.06g 92%) as a yellow oil. νmax 2115 (N_3), 1745 (CO), mass spectrum m/e 205 (M^+), (Found : C, 58.61; H, 5.40; N, 20.51; $C_{10}H_{11}N_3O_o$ requires C, 58.53; H, 5.40; N, 20.48); τ(CCl_4) 2.5-3.1 (aromatics, m) 5.7-6.1 (CH_2, q), 6.5 (CH_2,), 8.7-9(CH_3, t).

Reaction of Ethyl ester of 2-Azidophenylacetic acid with Hydrazine Hydrate

The ethyl ester of 2-azidopheny lacetic acid (2g) and hydrazine hydrate (2g) in ethanol was refluxed on a steam bath for 2h. On cooling white needles of the hydrazide of 2-azidophenyl acetic acid was formed. This was then filtered and washed with cold ethanol (30 ml) and dried. The yield was 1.77g (95%) (m.p. = 122°) νmax 3310 (NH), 2120 (N_3), 1645 (CO), (Found : C, 50.21; H, 4.74; N, 36.91; $C_8H_9N_5O$ requires C, 50.26; H, 4.74; N, 36.63), mass spectrum m/e 191 (M^+).

Reaction of N-(o-azidobenzoyl)aniline in Hydrazine

N-(o-azidobenzoyl)aniline (2.4g) in methanol (20 ml) containing hydrazine hydrate (2g) was heated under reflux for 10h. The solution was cooled and the ethanol was reduced to 10 ml and left to stand whereupon indazoline-3-one (0.88g, 65%) was formed. This was filtered, washed with cold ethanol (15 ml) and then dried (m.p. = 242°) (lit [194] 247°).

Reaction of Bis-N,N'-(o-azidobenzoyl)hydrazine with Hydrazine

Bis-N-N'-(o-azidobenzoyl)hydrazine (1g) in methanol (10 ml) containing hydrazine hydrate (1.5g) was refluxed on a steam bath for 8h. The mixture was then cooled and on standing overnight white rectangular plates of indazline-3-one was formed. The yield was 0.37g.

Reaction of 2-Azidobenzoic Anhydride with Hydrazine

2-Azidobenzoic anhydride (2.7) in methanol (10 ml) containing hydrazine hydrate (2g) was heated under reflux for 10 hrs. and on cooling indazoline-3-one (0.13g) was obtained. The ethanolic filtrate was then evaporated and this resulted in the formation of impure benzohydrazide which was confirmed by mixed melting point with authentic sample (m.p. = 124°).

Attempted Synthesis of 2-Azidobenzohydroxamic Acid

A solution of hydroxylamine in methanol was prepared by the addition of the calculated amount sodium methoxide (0.6g) in aqueous methanol (20 ml) to the hydroxylamine hydrochloride (0.7). To this solution was then added methyl o-azidobenzoate (1.63) and the mixture stirred for 24 hr. The methanol was then removed on a rotary evaporator and the white solid formed was filtered, washed with water, dried and recrystallised from benzene to give o-azidobenzoic acid (1.34g).

Preparation of Methy o-Nitrobenzenesulphonate

o-Nitrobenzenesulphonyl chloride (11g) was dissolved in dry ether (200 ml) in 500 ml flask. This was then placed in an icebath and to this was then added powder sodium methoxide (5g) in portions making certain that the temperature did not rise above 10^{o} after each addition. When this was complete, the mixture was stirred at room temperature for 12h. The solid formed was filtered, and the ether was removed on a rotary evaporator to give methyl o-nitrobenzenesulphonate (8.64g, 80%) (m.p. = 69^{o}).

Attempted Synthesis of Methyl 2-aminobenzenesulphonate

Methyl o-nitrobenzenesulphonate (10.5g) in methanol (300ml) was reduced separately with Raney-Nickel (10g) and Palladium charcoal (1g) in the presence of hydrogen in the autoclave for 10h. respectively. In each case the catalyst was removed by filtration and evaporation of the solvent produced a metal complex product which is now under further investigation.

A study of the rate of hydrolysis of Methyl Benzoate and Methyl o-azidobenzoate

Methyl benzoate (1g) and methyl o-azidobenzoate (1g) was each dissolved in 5N-sodium hydroxide (15 ml) and the solutions rapidly stirred. After 1 hr. extracts were taken from each solution, neutralized with HCl, and ether extracted. The etheral solutions were then dried over anhydrous magnesium sulphate and then examined on thin layer chromatographic plates. In the case of the azido-ester only one spot (eluting with light petroleum (b.p. 60-80°)) was obtained and this corresponded to that of 2-azidobenzoic acid whereas with the ester a mixture of methyl benzoate and benzoic acid was present. These products were confirmed by similar R_F values of authentic sample. Further investigation showed that the ester was completely hydrolysed after 24h.

BIBLIOGRAPHY

1) SCHMID, R.W., Helv. Chim. Acta., 45, 1982, (1962).

2) WOLFF, L., Ann., 59, 394, (1912).

3) HUISGEN, R. & APPL, M. Chem. Ber., 91, 1 and 12 (1958).

4) HUISGEN, R., Congress Handbook, XIII IUPAC Congress Zurich, 1955, p. 109.

5) HUISGEN, R., VOSIUS, D. & APPL, M., Angew. Chem., 67, 756, 1955.

6) APLL, M. & HUISGEN, R., Chem. Ber., 92, 2961 (1959).

7) Von E. DOERING, W. & ODUM, R.A., Tetrahedron. 22, 81, (1966).

8) JACKMAN, L.M., Application of N.M.R. Spectroscopy in Organic Chemistry. Pergamon Press, Lon. (1959).

9) MAIER, G., Angew. Chem., (Int. Edn.) 6, 402, 1967.

10) SUNDBERY, R.N. BRENNER, M., & SUTER, R., J. Amer. Chem. Soc., 79, 648, 1967.

11) ODUM, R.A. & BRENNER, M., J. Chem. Soc. (Suppl.) 1964, 5922.

12) SMITH, P.A.S., BROWN, B.B., PUTNEY, R.K. & REINISCH, R.F., J. Amer. Chem. Soc., 1953, 75, 6335.

13) HALL, J., BEHR, F., & REID, R., J. Amer. Chem. Soc., 2952, 1972.

14) OGATA, M., KANO, H. & MATSUMOTO, H., Tetrahedron. 25, 5205, 1969.

15) BERWICK, M.A., J. Amer. Chem. Soc., 93, 5730, 1971.

16) MAIR, A.C. & STEVENS, M.F., J. Chem. Soc., 2317, 1971.

17) BARKER, R.B., In Design of Active-Site-Directed Irreversible Enzyme Inhibitors, John Wiley, New York (1967).

18) ODUM, R.A. & WOLF, G., Chem. Comm., 360, 1973.

19) SMITH, P.A.S. & HALL, J.H., J. Amer. Chem. Soc., 84, 480, 1962.

20) HAFNER, K. & KONIG, C., Angew. Chem., 75, 89, 1963.

21) LWOWSKI, W., MARICICH, T.J. & MATTINGLY, J., J. Amer. Chem. Soc., 85, 1200, 1962.

22) LWOWSKI, W. & MARICICH, T.J., ibid., 87, 3630, 1960.

23) LWOWSKI, W. & JOHNSON, P.L., Tet. Letts., 891, 1967.

24) LWOWSKI, W. & McCONAGHY, J.S., J. Amer. Chem. Soc., 87, 5941, 1965.

25) LWOWSKI, W. & WOERNER, F.P., ibid., 87, 5491, 1965.

26) HAFNER, K., ZINSER, D. & MORITZ, K.L., Tet. Letts., 1733, 1964.

27) MARSH, F.D. & SIMMONS, H., J. Amer. Chem. Soc., 87, 3529, 1965.

28) COTTER, R.J. & BEACH, W.F., J. Org. Chem., 29, 751, 1964.

29) PAQUETTE, L.A. & BARRET, J.H., "Nonbenzoid Aromatics" ed. J.P. Snyder. Academic Press. New York & London, 1969, p. 254.

30) PAQUETTE, L.A. & DAWSON ibid., p. 354.

31) CHAPMAN, L.E. & ROBINS, R.F., Chem. Ind. (Lon), p. 1266, 1966.

32) BALDWIN, J.E. & SIMMONS, H., J. Amer. Chem. Soc., 89, 1886, (1967).

33) ABRAMOVITCH, R.A. & UMA, V., Chem. Comm., 707, 1968.

34) CADOGAN, J.I.G. & CAMMERON-WOOD, M., Proc. Chem. Soc., 1967, 361.

35) CADOGAN, J.I.G. & COOPER, A., J. Chem. Soc., (C) 883, 1963.

36) CADOGAN, J.I.G., CAMERON-WOOD, M., MAKIE, R.K. & SEARLE, R.J.G., J. Chem. Soc., 4831, 1965.

37) CADOGAN, J.I.G., MAKIE, R.K. & TODD, M.J., Chem. Comm., 491, 1966.

38) CADOGAN, J.I.G., KULIK, S. & TODD, M.J., ibid., 736, 1968.

39) KAMETANE, K., YAMANAKA, T. & OGASAWARA, K., — ibid., 966 (1968).

40) SMITH, P.A.S., & co-workers — J. Org. Chem., 23, 524, (1958).

41) CARBONI, R.A., CASTLE, J.E., KAUER, J.C. & SIMMONS, H.E., — ibid., 89, 2618, (1967).

42) KRBECHEK, L. & TAKIMOTO, H., — J. Org. Chem., 29, 1150, (1964).

43) ODUM, R.A. & BRUNNER, M., — J. Amer. Chem. Soc., 88, 2074, (1966).

44) CADOGAN, J.I.G. & TODD, M.J., — J. Chem. Soc., (C) 2808, (1969).

45) SUNDBERG, R.A., DIAS, B.P. & SMITH, R.H., Jr. — J. Amer. Chem. Soc., 91, 658, 1969.

46) CADOGAN, J.I.G. & MAKIE, R.K., — J. Chem. Soc., (C) 2819, (1969).

47) ATHERTON, F.R. & LAMBERT, R.W., — J. Chem. Soc., (Perkin 1). 1079, (1969).

48) SUNDBERG, R.J. & SMITH, R.H. Jr. — Tet. Letts.

49) KWOK, R. & PRANC, P., — J. Org. Chem., 33, 2880, (1969).

50) OGATA, M., KANO, H. & MATSUMOTO, H., — Chem. Comm., 397, (1968).

51) Von HEINZELMANN, W. & MARYY, M., — Helv. Chim. Acta. Vol. 56, Fras 6, 1852, (1973).

52) PAQUETTER, L.A., KUHLA, D.E., BARETT, J.H., & HALUSKA, R.J., — J. Chem. Soc., 34, 2866, (1969).

53) HASSNER, A., LORBER, M.E. & HEATHCOCK, C., — J. Org. Chem., 32, 540, (1967).

54) GEBELEIN, C.G. & SEVERN, D. — ibid., 32, 3665, 1967.

55) DRΞFAHL, G. & PONSOLD, K., — J. Prakt. Chem., 23, 136, (1964).

56) PAQUETTE, L.A. & KUHLA, D.E., — Tet. Letts., 4517, (1967).

57) PAQUETTE, L.A. & KUHLA, D.E., — "Non-Benzenoic Aromatics" ed. J.P. Snyder. Academic Press, New York & London 1969, Vol. 1, p. 256.

58) PAQUETTE, L.A. & HALUSKA, R.J., ibid., Vol. 1, p. 256.

59) PAQUETTE, L.A., BORRETT, J.H. ibid., Vol. 1, p. 256.

60) MEYER, E. & GRIFFIN, G. Agnew. Chem., 79, 648, (1967).

61) SPILITTER, J.S. & CALVIN, M., Tet. Letts., 1445, (1968).

62) PRINZBACH, H., FUCHS, R. & KITZING, R., Angew. Chem., (Inter. Edn.) 7, 67, (1968).

63) CHILDS, R.T. & JOHNSON, A.W., Chem. Comm., 95, 1965.

64) CHILDS, R.T. & JOHNSON, A.W., J. Chem. Soc., (C), 1950, (1966).

65) ANDERSON, M. & JOHNSON, A.W., J. Chem. Soc., 2411, 1965.

66) PAQUETTE, L.A., J. Amer. Chem. Soc., 85, 3288, (1963).

67) PAQUETTE, L.A. & FARLEY, A.W. ibid., 89, 3595, (1967).

68) PAQUETTE, L.A. ibid., 85, 4053, (1963).

69) PAQUETTE, L.A. ibid., 86, 4096, (1964).

70) VOGEL, E. & ERD, R., Angew Chem., 74, 76, (1962).

71) VOGEL, E., ERB, R., LENZ, G. & BOTHNER-BY, A.A., Ann. 1, 682, (1965).

72) GUNTHER, H. & WENZL, R., Tet. Letts. 4155, 1967.

73) PAQUETTE, L.A. & MALPASS, J.R., "Non-Benzonoid Aromatics" ed. J.P. Snyder, Academic Press, New York & London, Vol. 1, p. 281.

74) PAQUETTE, L.A. & HALUSHA, R.J., Chem. Comm., 1370, 1968.

75) OKAMURA, W.H., SNIDER, W.H. & KATZ, T.J. Tet. Letts., 3367, (1968).

76) WASSERMAN, E., MURRAY, R.W. YAGER, W.A., TROZZOLO, A.M. & SMOLINSKY, G., J. Amer. Chem. Soc., 89, 5076, (1967).

77) RIESER, A., WILLETS, F.W., TERRY, C.G. WILLIAMS, V. & MARLEY, R., Trans. Farad. Soc., 64, 3265, (1968).

78) WALKER, P. & WATERS, W., J. Amer. Chem. Soc., 73, 2435, (1951).

79) SMITH, P.A.S. & BROWN, B.B., ibid., 73, 2435, (1951).

80) ABRAMOVITCH, R.A. & SCRIVEN, E.V., Chem. Comm., 789, 197

81) BAMBERGER, E., Ann. 443, 192, (1925).

82) METH-COHN, O., SMALLEY, R.K. & SUSCHITZKY, H. J. Chem. Soc., 1666, (1963).

83) SMALLEY, R.K. & SUSCHITZKY, H., ibid., 5571, (1963).

84) ASHBY, J., SCRIVEN, E.F. & SUSCHITZKY, H., J. Chem. Soc. (D) 366, 1972.

85) CADOGAN, J.I.G. & KULIK, S., J. Chem. Soc., (C) 2621, 1967 and references cited therein.

86) SMITH, P.A.S. & BROWN, B.B., J. Org. Chem. 23, 524, 1958.

87) OAKWOOD, T.S. & WEISGERBER, C.A. Org. Synthsis. 1965, (Coll. Vol. 3), p. 112.

88) O'SULLIVAN, D.G. J. Chem. Soc., 3278, 1960.

89) EDWARDS, J.T., ibid., 222, (1956).

90) GARNER, R., MULLOCK, E.B. & SUSCHITZKY, H., J. Chem. Soc., (C), 1980, (1968).

91) HEIN, D.W., ALHEIM, R.J. & LEAVITT, J.J. J. Amer. Chem. Soc., 79, 427, (1957).

92) MITIN, YU. V. & VLASOV, G.R., Probl.Org.Sinteza., 27, 304, (1965).

93) GAUGHRAN, R.T., PICARD, J.P. & KAUFMAN, J.V.R. J. Amer. Chem. Soc., 76, 2333, (1954).

94) SMITH, P.A.S. & BOYER, J.H., Org. Synthesis. 1963, (Coll. Vol. IV)., p. 75.

95) BIRKHIMER, E.A., NORUP, E.A. & BAK, T.A., Acta, Chem. Scand., 14, 1894, (1960).

96) DYALL, L.K. & KEMP, J.E., J. Chem. Soc., (B) 976, (1968).

97) CHATTAWAY, F.D. & ORTON, K.J.P., J. Chem. Soc., 1046, (1899).

98) SHEINER, P., SCHOMAKER, J.H., DEMING, S., LIBBEY, W.J. & NOWACK, G.P., J. Amer. Chem. Soc., 87, 306, (1965).

99) PRITZKON, W. & TIMM, D., J. Prakt. Chem., 32, 178, (1966).

100) SMOLINSKY, G., SNYDER, L.C. & WASSERMAN, E., Rev. Mod. Phys. 35, 576, (1963).

101) REISER, A., WAGNER, H. & BOWES, G., Tet. Letts. 23, 2365, (1966).

102) FOWLER, F.W. & HASSNER, A.W. J. Amer. Chem. Soc., 90, 2875, (1968).

103) ABRAMOVITCH, R.A., CHALLAND, S.R. & SCRIVEN, E.V., J. Org. Chem. 37, 2705, (1972).

104) ABRAMOVITCH, R.A. & CHALLAND, S.R., J. Chem. Soc., (D) 964, (1972).

105) "Benoxazoles and Related Systems", "Heterocyclic Compounds", edition R.C. Elderfield, Vol. 5, p. 418.

106) HEWIT, L.F. & KING, H., J. Chem. Soc., 817, 1926.

107) NEWBERY, G. & KING, M.A. ibid., 116, 1928.

108) SATO, S., Rippon Kagaku Zasshe, 90, 113, (1969).

109) GREISS, P., Ber., 19, 313, (1886).

110) SUNDBERG, R.J. & SMITH, R.H. Jr., J. Org. Chem., 39, 93, 1974.

111) SWENTON, J.S., Tet. Letts., 3421, 1969.

112) SMALLEY, R.K. & BINGHAM, T.E., J. Chem. Soc., (C) 2481, 1969.

113) PATAI, S., & GOTSHAI, Y., J. Chem. Soc., (B) 489, (1966).

114) ZINCKE, T. & LAWSON, A.T., Ber., 20, 1176 (1887).

115) ZINCKE, T. & JAENKE, H., ibid., 21, 546, (1888).

116) SMOLINSKY, G., J. Org. Chem., 83, 2489, (1961).

117) KATRIZKY, A.R., BOULTON, A.J. & GHOSH, P.B., J. Chem. Soc., (B) 1011, (1966).

118) KREBECHECK, L. & TAKIMOTO, H., J. Org. Chem., 29, 2630, 1964.

119) BAMBERGER, E. & DEMUTH, E., Ber., 34, 3874, 1901.

120) GATTERMAN, L. & EBERT, E., ibid., 49, 2117, 1916.

121) SMITH, P.A.S., HALL, J.H. & KAN, R.O., J. Amer. Chem. Soc., 84, 485, 1962.

122) RAO, K.A.N. & VENKATARAMAN, P.R. J. Indian Chem. Soc., 15, 201, 1938.

123) DYALL, L.J. & KEMP, J.C., Aust. J. Chem., 20, 1625, (1967).

124) LEYSHON, L.J. & SAUNDERS, D.G., Chem. Comm. 1608, (1971).

125) BAMBERGER, E. & DEMUTH, E., Ber., 35, 1885, (1902)

126) VOGEL, A.I., Pract. Org. Chem., (Third Ed.) 1966, 792.

127) RUPE, H. & MAJEWSKI, C., Ber., 33, 3405, (1900).

128) NAKANISHI, K., "Infrared Absorption Spectroscopy" ed. Nankod Comp Ltd., Tokyo, p.60.

129) SMALLEY, R.K. & SUSCHITZKY, H., J. Chem. Soc., 755, 1964.

130) BAMBERGER, E. & PYMAN, F.L., Ber. 42, 1368, (1909).

131) SUNDBERG, R.J. & SLOAN, K., J. Org. Chem., 38, 2052, 1973.

132) FELT, G.R., LINKE, S. & LWOWSKI, W., Tets. Letts., 2037, (1972).

133) ODUM, R.A. & AARONSON, A.M., J. Amer. Chem. Soc., 91, 5680, 1969.

134) SUNDBERG, R.J. & SMITH, R.H., Jr. J. Org. Chem. 36, 295, 1971.

135) BRESLOW, D.S. & EDWARDS, E.I., Tet. Letts., 2041, (1972).

136) CADOGAN, J.I.G. Private Communications, University of Edinburgh.

137) VOGEL, E. & ERB, R., Angew. Chem., (Intern. Ed.) 53, 1, 1962.

138) SAUNDER, M. & GOLD, E.H., J. Org. Chem., 27, 1439, (1962).

139) KAPLAN, F. & ROBERTS, J.D., J. Amer. Chem. Soc., 1964, 83, 4666.

140) WHITESIDES, G.M., KAPLAN, F., & ROBERTS, J.D., — Proc. Natl. Acad. Sci., U.S.A. 1962, 48, 1112.

141) ELVIDGE, J.A. & FOSTER, R.G., — J. Chem. Soc., 981, 1964.

142) MEYER, W.L. & co-workers — J. Amer. Chem. Soc., 87, 1573, (1967).

143) WHITESIDES, G.M., HOLTZ, D. & ROBERTS, J.D., — ibid., (1964), 86, 2628.

144) RINEHART, Jr. K.L., BUCHHOLZ, A.C. & Van LEAR, G.E., — ibid., 1073, 90, 1968.

145) REES, C.W. & co-workers — J. Chem. Soc., (C) 981, 1971.

146) MEYER, R. & MAIER, J., — Ann., 46, 327, 1903.

147) CADOGAN, J.I.G., MARSHALL, R., SMITH, D.M. & TODD, M.J., — J. Chem. Soc., (C) 2441, (1970).

148) SMOLINSKY, G. — J. Org. Chem., 26, 4108, (1961).

149) HORNER, L., CHRESTMANN, A. & GROSS, N., — Chem. Ber., 96, 399, 1963.

150) REISER, A. & co-workers — Trans. Farad. Soc., 64, 3265, 1968.

151) GIBSON, H.H., BRUNDY, C.H., & GRADY. 111, H.R. — Tet. Letts., 1973, 3801.

152) SMITH, P.A.S., — "Nitrenes" ed. W. LOWOSKI, John Willey & Sons, New York, N.Y. 1970, p. 114-119.

153) KYM, O., — J. Pv. Chem. 75, 322, (1907).

154) MISTRY, S.M. & GUHA, P.C., — J. Ind. Chem. Soc., 7, 493 (1930).

155) ASHBY, J. & SUSCHITZKY, H. — Tet. Letts. 1971, 1315.

156) LEFFLER, J.E. & GIBSON, H.H. — J. Amer. Chem. Soc., 90, 4117, (1968).

157) CARBONI, R.A. & CASTLE, J.E., — ibid., 84, 2435, (1962).

158) HALL, J.H., — ibid., 87, 1147, (1965).

159) ABRAMOVITCH, R.A. & DAVIS, B.A., — Chem. Rev., 64, 149, (1964).

160) BRADBURY, S., KEATING, M., REES, C.W. & STORR, R.C., Chem. Comm., 1971, 827.

161) PEEK, M.E., REES, C.W. & STORR, R.C., J. Chem. Soc., Perkin I 1260, (1974).

162) PERGOTTI, A. & CONTARDI, M.A., Gazz. Chim. Ital., 32, I, 573 (1962).

163) MANGANI, A. & DALMONTE-CASONI, D., Boll. Sci. Fac. Chem. Ind. Bologna, 3, 173, (1942).

164) FOSTER, M.O. & FIERZ, H.C., J. Chem. Soc., 91, 1942, (1907).

165) HILL, D.L., HO, K.C. & MILLER, J., J. Chem. Soc., (B) 299, 1966.

166) FULLER, M.W. & MILLER "Chemistry of the Azido Group" ed. S. Patai Interscience Publishers, John Willey & Son, London, New York, 1971, p. 212.

167) CLUSIUS, K. & HURZERTER, H., Helv. Chim. Acta, 37 798, 1954.

168) CLUSIUS, K. & VECCHI, M., ibid., 39 1469, (1956).

169) Von ROTHERBURG, R., Ber., 26, 2060, (1893).

170) RUPP, H.D., DISSERTATION, University of Wurzberg 1964.

171) DARAPSKY, A., Ber., 40, 3036, (1907).

172) FOSTER, M.C., J. Chem. Soc., 89, 222 (1906).

173) ZINCKE, T. & SCHWARZ, P., Ann., 307 28, (1899).

174) BAMBERGER, E. & RENAULD, Ber., 30, 2288 (1898).

175) TEITER, H.M. & BELL, E.W., Organic Synthsis, 1963, (Coll. Vol. IV), p. 125.

176) HODGSON, H.H. & KERSHAW, A., J. Chem. Soc., 192, (1928).

177) HUNN, E.B., J. Amer. Chem. Soc., 45, 1024, (1923).

180) ADAMS, R. & co-workers ibid., 48, 1758, (1926)

181) PURGOTTI, A. & CONTARDI, M.A., Gazz. Chim. Ital. 32, I, 534, (1962).

182) LELLMAN, E. & WURTHER, R., Ann., 228, 212, 1896.

183) BAMBERGER, E., Ber., 35, 3895, (1903).

184) VOGEL, A.I., "Elementary Pract. Organic Chemistry", Part 2 - publishers, Longmans, 1968, p. 390.

185) VOGEL, A.I., ibid.,p. 390.

186) VOGEL, A.I., ibid.,p. 393.

187) VOGEL, A.T., ibid.,p. 393.

188) MEYER, F., DAHLER, K., Ann. 326, 346 (1903).

189) BIGIAVI, D., GUARDUCCI, M., Gazz. Chim. Ital., 57 156 (1927).

190) LEUCHS, H., Ber., 40, 1085 (1907).

191) WHITT, F.H., Ber., 45, 2380 (1912).

192) KURAS, M., Coll. Czech. Chem. Abst., 11, 313, (1939).

193) FOSTER, M.O. & FIERZ, H.E. J. Chem. Soc., 1352, (1907).

194) FISCHER, E., Ber., 13, 697 (1880).

195) BAEYER, A. & KNAP, J., Ann. 140, 1 (1866).

Tetrahedron Letters No. 10, pp 825 - 828, 1974. Pergamon Press. Printed in Great Britain.

THERMOLYSIS OF ARYL AZIDES IN BENZOYL CHLORIDE

R. K. Smalley*, W. A. Strachan and H. Suschitzky,
Department of Chemistry and Applied Chemistry,
University of Salford, Salford M5 4WT, Lancashire.

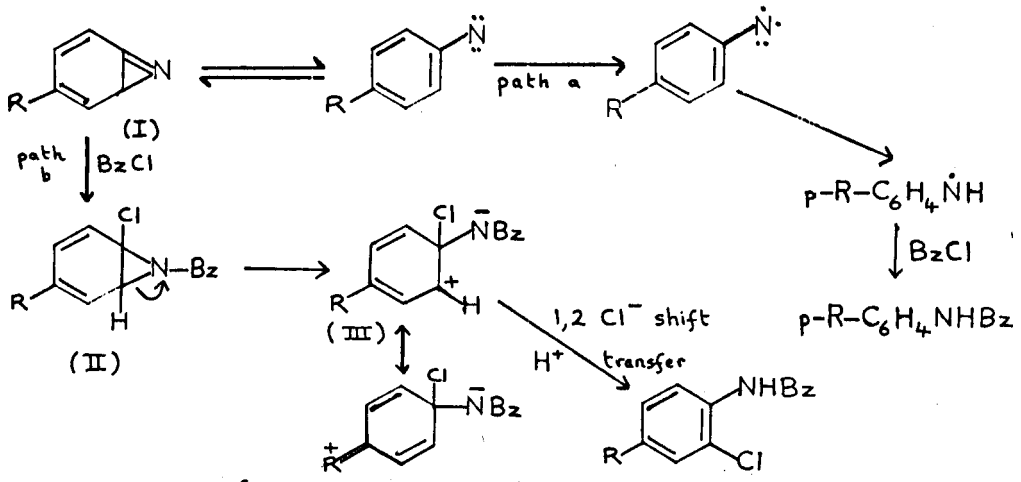
(Received in UK 4 January 1974; accepted for publication 28 January 1974)

In continuation of our studies[1] on the decomposition of aryl azides in various solvents, we thermolysed various aryl azides in boiling benzoyl chloride with results given in the Table.

As expected, o-nitrophenyl azide and o-azidobiphenyl yielded benzofuroxan and carbazole respectively, while p-nitrophenyl azide gave only tars. In the other examples, the formation of azo-compounds and substituted benzanilides is probably due, particularly in the latter case, to triplet nitrene[2] participation (see Scheme; path a)[3]. However, the reasons for o-chlorobenzanilide[4] formation in the case of phenyl, p-methylphenyl, and p-methoxyphenyl azide are less obvious. If, as anticipated, the nitrene was first inserted into the carbon-halogen bond of the acyl halide, then the resulting N-chlorobenzanilide (ArN(Cl)COPh) would have to undergo an ortho Orton-type rearrangement. However, Orton has reported[5] that N-chlorobenzanilide on thermolysis in an inert solvent yields only p-chlorobenzanilide. We have confirmed this result and also shown that the N-chlorobenzanilide behaves similarly in boiling benzoyl chloride. The possibility of a radical or electrophilic chlorination yielding o-chloro-anilides is unlikely because of the high ortho selectivity of the halogenation process. For instance, o-methoxyphenyl azide in boiling benzoyl chloride gave 2-chloro-6-methoxybenzanilide and much tar from which no products could be isolated. Photolysis of the azides in benzoyl chloride gave the same products in much reduced yield. For example, 4,4'-dimethoxyazobenzene (2%) and 2-chloro-4-methoxybenzanilide (20%) were obtained by irradiation of p-methoxyphenyl azide for 24 h. (medium pressure 100 W. lamp).

We propose a mechanism as outlined in the reaction scheme (path b) which explains our results and rationalises the fact that the yield of o-chloro-anilide diminishes with a decrease in the electron donation of the para substituent (i.e., MeO > Me > H > Cl).

SCHEME



There is evidence[6] that the initially formed singlet nitrene is in equilibrium with the azirine (I), and as such can react with benzoyl chloride to give the adduct (II). When substituent R is electron donating, (i.e., Me, MeO, and to a lesser extent, H), the aziridine intermediate (II) opens, not by an electrocyclic process as in the case of azepine formation[7], but by heterolysis of the C-N bond to give the resonance stabilised dipolar species (III). A 1,2-chloride ion shift[8] and proton transfer then yields the o-chlorobenzanilide. Similar reactions have been invoked to explain the intermolecular substitution reactions of aryl-, sulphonyl-, ethoxycarbonyl-, and cyanonitrenes with aromatic substrates[9]. That o-chlorobenzanilide is a reaction of singlet nitrene was demonstrated by carrying out the decomposition of phenyl azide in boiling benzoyl chloride under oxygen, a well-known triplet quencher. o-Chlorobenzanilide was obtained in undiminished yield, whereas triplet based products, such as benzanilide, were isolated in much reduced amounts (20%), and azobenzene could not be detected.

The above considerations may throw new light on the formation of o-aminophenols, in the decomposition of aryl azides in acetic anhydride[1a]. Although N,O-diacylhydroxylamines, which we postulated as first step in this decomposition, undergo thermal rearrangement to o-aminophenols[10], we now favour a pathway analogous to the one proposed above (i.e., addition of acetic anhydride to the azirine[11] followed by ring opening to give the rearranged product).

TABLE

Decomposition of Aryl Azides in Boiling Benzoyl Chloride[a]

Azide	Products	Yield (%)
PhN_3[b]	azobenzene	2
	benzanilide	50
	2-chlorobenzanilide	11
p-$MeC_6H_4N_3$	4,4'-dimethylazobenzene	2
	4-methylbenzanilide	34
	2-chloro-4-methylbenzanilide	19
p-$MeOC_6H_4N_3$	4,4'-dimethoxyazobenzene	6
	2-chloro-4-methoxybenzanilide	67
p-$Cl.C_6H_4N_3$	4,4'-dichloroazobenzene	9
	4-chlorobenzanilide	24
p-$NO_2C_6H_4N_3$	tars	-
o-$MeOC_6H_4N_3$	2-chloro-6-methoxybenzanilide	55
o-$NO_2C_6H_4N_3$	benzofuroxan	83
o-$N_3.C_6H_4.C_6H_5$	carbazole	75
	N-benzoylcarbazole	10

[a]Decompositions were carried out in freshly distilled deoxygenated benzoyl chloride under dry nitrogen.

[b]A low yield (ca. 2%) of 6-chloro-2-phenylbenzoxazole was also isolated. The origin of this interesting by-product is being investigated.

REFERENCES

1. R. K. Smalley and H. Suschitzky, J. Chem. Soc.; a) 1963, 5571; b) 1964, 5922.
2. P. A. S. Smith in "Nitrenes", ed. W. Lwowski, Interscience Publishers, 1970, p.99.
3. Kinetic data indicate that nitrene formation occurs without solvent participation.
4. The identity of all reaction products was established by unambiguous synthesis and the usual spectral data.
5. F. D. Chattaway and K. J. P. Orton, J. Chem. Soc., 1899, 75, 1046.
6. F. R. Atherton and R. W. Lambert, J. Chem. Soc. Perkin I, 1973, 1079, and references cited therein.
7. R. Huisgen and M. Appl, Chem. Ber., 1958, 91, 1 and 12.
8. Chloride ion migration may be synchronous with aziridine ring opening.
9. R. A. Abramovitch, S. R. Challand and E. F. V. Scriven, J. Org. Chem., 1972, 37, 2705. and references cited therein.
10. L. Horner and H. Steppan, Annalen, 1957, 606, 24.
11. The addition of acetic anhydride and benzoyl chloride to 1H-azirines is well documented; see F. W. Fowler, Advances in Heterocyclic Chemistry, 1971, 13, 67.